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SOME RECENT TRENDS IN NEUROPATHOLOGY

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IN his presidential address to the first International Congress of Neuropathology in Rome, Gozzano (1952) raised the question of the future of neuropathology. In his opinion neuropathology was a relatively young branch of pathology and had started with the discoveries of Golgi, Cajal, Weigert and Nissl. Golgi invented "la reazione nera" in 1873; it was applied to the nervous system only a decade later. The first Weigert preparations for myelin were demonstrated in 1884 (Wallenberg, 1925). Nissl, inspired by Weigert's success with aniline dyes in nerve fibres, introduced his method for nerve cells in 1885, using first magenta red, later methylene blue and finally toluidine blue. Cajal made his first scientific appearance in 1889, at a meeting of the German Society of Anatomists.

Neuropathology had its heyday at about 1900 and in the first two decades of this century, which had witnessed first the conquest of the cerebral cortex, and then of the basal ganglia and the grey matter round the third ventricle. Since then the flow has become broader, but also appreciably slower. It is true that more recently much important work has been carried out in the field of vascular pathology, anoxia and oedema, encephalitis, allergy, nutritional deficiencies, tumour, and—especially—comparative neuroanatomy and neuropathology—to mention only a few. It is equally true, however, that there have been relatively few spectacular advances in the last twenty years, a period in which profound advances have been made in the other basic sciences such as biochemistry, biophysics, physiology and endocrinology. More and more, neuropathologists have concerned themselves with the filling of gaps or with disputation over lesser diagnostic detail. As Gozzano puts it, the "disquieting" question thus presents itself, whether the period of neurohistology is coming to a close and is being superseded by neurochemistry and neurophysiology. Perhaps this problem has nowhere arisen with greater urgency than in the pathology of mental disease, since the majority of psychoses, the schizophrenias, manic-depressive insanity, many symptomatic psychoses and the higher grades of mental defect are still left without a generally accepted somatic substrate.

DEVELOPMENT OF MORPHOLOGICAL RESEARCH ON THE BRAIN

One might question Gozzano's assessment of the age of neuropathology. Korn (1903), in the only *History of Neuropathology* known to the present writer, dates the effective beginning of neuropathology in the early decades of the 19th century when substantial neurohistological discoveries were made. However, concrete and important *macroscopic* observations had been reported much earlier, for example, by Wepfer (1658) who seems to have been the first to describe haemorrhage in the brain of apoplectics; by Willis (1672) who connected motor paralysis with lesions in the region of the corpus striatum; furthermore, by Bonetus (1679, 1700) and Morgagni (1761), to mention only a few. In the psychiatric monographs of the second half of the 18th century, post-mortem findings in mental patients were frequently mentioned; we owe systematic contributions especially to Greding (1781, 1790), Haslam (1798), Crowther (1811) and Andrew Marshal (1815). A fuller account of these early developments will be found in the present writer's Maudsley lecture (Meyer, 1960).

Microscopes began to be developed early in the 17th century. By the time of the publication of Willis's important books, there had already arrived what Singer (1950) has called the "classical microscopists": two Englishmen (Hooke and Grew), two Dutchmen (van Leeuwenhoek and Swammerdam) and the Italian Malpighi. Much of their work was published in English by the Royal Society. Malpighi demonstrated the capillary system in the frog's lung; Grew investigated the sexual organs in plants. To Leeuwenhoek goes the merit of having discovered the blood corpuscles and their nuclei; Hooke described the constituent microscopic structures of cork, the walls of which he referred to as "cells", and Swammerdam's *biblia naturae* is, according to Singer, "the finest collection of microscopical observations ever produced by a single worker". There is no adequate explanation why these fine early achievements were not followed up in the next century and, in particular, why, during this period, there was little or no successful work on nervous tissue. It may be that there was so much to be discovered about plants and unicellular organisms that there was little inclination to think of anything more specialized. Robert Hooke writes in his *Micrographia* that the microscope makes some men "excell others in their observations and deductions almost as much as they do the beasts"; the complexity of living things thus revealed was as disturbing in its novelty as the astronomical world of Galileo and Kepler. I quote this from Singer, who also points out that the "classical" microscopists were all rather peculiar and withdrawn people of poor general health and—some—also of poor mental health. They had no pupils who could have passed on and spread their discoveries. Moreover there was a widespread belief (first expressed by Malpighi (1669), but still conspicuous in the writings of Boerhaave (1708) and others in the 18th century) that nervous action consists of the propulsion of a subtle fluid which was not accessible to microscopic investigation. Although alcohol had previously been used for the preservation of biological specimens, Reil (1809) seems to have been the first to suggest its application to nervous tissue (Papez, 1953).*

One or all of these reasons may have been responsible for the retardation of

* Chromic acid salts were not introduced before 1844 by Hannover and formalin much later by Blum (1893). Embedding in paraffin was introduced by Klebs in 1869, and was supplemented by collodion (Duval, 1879) and celloidin (Schiefferdecker, 1882). Stilling (1842) devised a primitive microtome for serial sectioning by hand and von Gudden (1875) introduced his famous microtome for sectioning the whole hemisphere. Carmine, advocated by Gerlach in 1858, remained for a long time the standard staining method (Long, 1928; Papez, 1953; and Neubuerger, 1953).

neurohistology, but once the immense technical difficulties and mental prejudices were overcome, epoch-making discoveries followed. Pre-eminent among those who used the new compound microscope for the study of nervous tissue were Ehrenberg, Valentin, Purkinje, R. Remak, Schwann and Schleiden. They all had in common a remarkable gift for accurate and sober observations which were achieved by (compared with modern standards) primitive dissection techniques and without the use of staining methods.

Their work much overlapped which makes it often difficult to apportion priorities. However, to Ehrenberg (1836) goes the merit of having first described and illustrated nerve cells in the spinal ganglia. This is attested by Remak (1838), Schwann (1839), Waldeyer (1891), von Töply (1903), as well as by Spatz (1929). In 1838 Purkinje was already able to publish a brief account of results, which included what Bartelmez (1953) called the first adequate description of nerve fibres and nerve cells in the brain with their dendrites, among them the flask-like "Purkinje cells". In the same year, Remak showed his familiarity with the "Ganglienkugeln" and their nuclei and nucleoli. Before Schwann, he had already demonstrated (1836, 1837a) myelinated and unmyelinated (primitive) nerve fibres, acknowledging the part played by his teacher Ehrenberg in these discoveries. Schwann soon (1839) confirmed and amplified Remak's findings concerning the myelin sheath and, in addition, clearly described and illustrated the neurilemmal sheath containing the nucleated cells which bear his name.

Among other early and penetrating observations, we find Remak's (1837b) description of fibre plexus ("darmförmige Schlingen") around nerve cells; although he failed to demonstrate the actual endings on the nerve cell, he was fully aware of the significance of this intimate spatial relationship. He also saw (1837c) a bundle, arising from one aspect of the nerve cell, which he thought to be composed of primitive fibres. Later (1844) he observed delicate primitive fibres running through the substance of the "Ganglienkugel" to join this bundle; possibly the first mention of neurofibrils, although accurate observation of these structures was only achieved later by M. Schultze (*vide* Spatz, 1929). In the same paper, Remak gives a diagrammatic illustration of the cerebral cortex distinguishing—like Baillarger four years earlier—six layers of which the outermost is white and the remainder alternately grey and white.

The neuroglia was described—somewhat later—by Virchow. In 1854, this author mentioned, in passing, "a soft mass, belonging to the category of mesodermal tissue which penetrates and sustains the nervous elements, the ependyma being its surface part" (present author's translation). Two years later (1856) Virchow gave a fuller and surprisingly accurate description of this "Kitt" (neuroglia) which consists of nuclei embedded in cells with soft and frail cytoplasm, forming, in pathological conditions, the fat-laden compound granular cells ("Körnchenkugeln") and a dense fibrous band beneath the ventricular (and cortical) surfaces.

Notwithstanding these early triumphs, the relationship between nerve cells and nerve fibres remained obscure and was the object of intense research. The neurone theory received its definitive formulation only about 50 years later by Waldeyer (1891) who coined the term "neurone". It is interesting to note in his historical review that, as early as the 1840's, Remak (as already mentioned), von Köllicker and others came very near the truth. Deiters, in 1865, clearly demonstrated the origin of nerve fibres from anterior nerve cells. The final dénouement was initiated by the introduction of Golgi's method, which played an important part in Cajal's early contributions to the problem between 1889 and

1891, and by the work of Forel (1887) and His (1887). The theory was not generally accepted in the first decades of the 20th century, Cajal being its most important protagonist, while Nissl (1903), among others (including Golgi himself), remained unconvinced.

The striking developments in neurohistology had their counterpart in the field of pathology. Gross lesions such as haemorrhage, meningitis, abscess, tuberculoma and tumours had been known for a long time. One of the early achievements of the 19th century was the clinico-pathological concept of general paralysis. The clinical picture of this disease had been outlined by Haslam in 1798 (his Case 15), but the merit for establishing the condition on a firmer basis of clinico-pathological experience goes to Bayle (1822, 1826), Calmeil (1826) and other disciples of Esquirol. A macroscopic description of tabetic degeneration was given with surprising accuracy by Romberg in 1851. The atrophy of the brain in demented senile persons also attracted early attention (e.g. that of Calmeil), and McMenemey (1958) quotes the careful post-mortem observations made by Webster in the mid-19th century on cases of dementia developing in middle and old age. In Andrew Marshal's book (1815) (as previously in the writings of Willis (1672), Harper (1789) and Crichton (1798)), we find frequent references—in cases of mania—to patchy ossification of arteries, undoubtedly including arteriosclerotic disease. As McMenemey points out, work on arteriosclerosis was stimulated later by Virchow and his school and in the closing decades of the 19th century also attracted the systematic attention of neuropathologists.

In 1835, Cruveilhier gave his classical macroscopic description of disseminated sclerosis, repeated by Carswell (1838),* but elaborated with the help of the microscope only later by Charcot (1868). The latter and his associates were also responsible for the first clinico-anatomical description of amyotrophic lateral sclerosis (Charcot 1865, Charcot and Joffroy, 1869).

Other important investigations of Charcot and his collaborators included the histopathology of *tabes dorsalis* and of miliary cerebral aneurysms, and the first description of anterior horn atrophy in infantile paralysis (de Morsier, 1953; Guillain, 1955).

Here should also be mentioned the microscopic investigations on secondary degeneration undertaken by Waller in 1850, a problem to which Türck (1849-1853) also made important contributions; furthermore, the investigations on system degeneration carried out clinically (in the 1850's and 1860's) by Duchenne and, pathologically, by N. Friedreich (1863).

After the eclipse of the phrenological schools, Flourens (1824, 1842) dominated the scene with his view of the equi-potentiality of function within the cerebral cortex. Against this background arose the series of important discoveries of specific localization, beginning with Broca's discovery (1861) of expressive speech disturbed by lesions of the posterior third frontal convolution†, followed by that of "word deafness" (Bastian 1869), of sensory aphasia (Wernicke, 1874), of the motor cortex (Fritsch and Hitzig, 1870, Ferrier, 1874), of focal epilepsy (Jackson, from 1864 onward); temporal lobe epilepsy (Jackson, 1888), visual

* One finds in Carswell's book (his chapter on atrophy) also what is probably the first anatomical description of the lesions of general paralysis in English, but with no indication whether this was his independent observation or taken over from French findings. De Morsier mentions that Carswell had previously been in Paris where he might possibly have seen both Cruveilhier's and Bayle's findings.

† Broca was indirectly influenced by the teaching of Gall whose pre-eminence in the early development of regional localization in the brain has been re-emphasized recently by Grünthal and Strauss (1949), Jefferson (1953) and Ackerknecht (1958).

cortex (Nothnagel, 1879, Henschen, 1893), the frontal lobe syndrome (Harlow, 1848, Ferrier, 1878, Welt, 1887), the importance of the temporo-parieto-occipital association areas for mental life, based on myelogenetic studies which Flechsig (1876) undertook from 1872 onwards—to mention only some landmarks in a brilliant sequence which still continues with undiminished élan in our own day. Although some of the work was experimental, most discoveries were made in clinico-pathological observations of patients. They were true neuropathological contributions, though in the early days achieved without the aid of the microscope.

THE PRESENT PHASE OF NEUROPATHOLOGY

I have dwelt on the earlier phases of development at some length in order to show that the idea of structural integrity of the central nervous system as a prerequisite of mental and nervous function is an old one. The concept had developed during the 17th and 18th centuries, slowly, with many interruptions and still tainted with ancient “animistic” beliefs. The pace quickened with the beginning of the 19th century, and before and soon after the mid-century many—for that time epoch-making—discoveries were made in normal and morbid anatomy. The era which opened in the closing decades of the century was certainly not a “young” branch of pathology; rather would one liken it to the gathering of the harvest and consider it the autumn of a predominantly morphological approach. There were several reasons why this new phase began at about this time: in the first place enough of the factual foundations had been laid for new men of genius, Golgi, Cajal, Nissl, Weigert and Etinger to build upon. But the more important cause was probably that physical and chemical advances had by that time reached a stage favourable for the development of more adequate techniques and for more refined interpretation of pathological lesions. It is no coincidence that the modern microscope was born in 1878 when the Zeiss firm in Jena began to construct models designed by E. Abbé, who ten years later, became the director of the firm and introduced the new sub-stage condenser which bears his name and which had great influence on the spread of microscopic research (Singer, 1950). With von Gudden began a new era in the development of microtomes and, although Nissl in his earlier years is reputed to have cut his sections by hand with a razor, the appearance on the market of precision instruments greatly facilitated histological accuracy. Even more important was the introduction of metallic impregnation by Golgi and Cajal and of aniline dyes by Nissl and Weigert. Of Weigert Alzheimer used to say that it was this master who created all the tools for neurohistology (Neubuerger, 1953). Although most of these staining methods aimed at making structure visible and, for this reason, were not strictly speaking histochemical, nevertheless they were bound to reveal chemical and physical properties of the components of nervous tissue and were, in a broad sense, the forerunners of modern histochemistry. They probably represent all that chemistry of the brain at that time had to offer for the investigation of nervous tissue. Histochemical thought, as Einarson (1957) reminds us, can be detected in the investigations of Nissl bodies, which were classed by Held as nucleoproteins as early as 1895.

The enormous strides of biophysics and biochemistry during the last fifty years are likely to influence the future development of the histopathology of the nervous system even more profoundly than at the turn of the century.

Neuropathologists, with few exceptions, have been slow to take cognizance of the changing situation; much slower, in fact, than neuroanatomists, who—

in English-speaking countries, at least—have widely adopted neurophysiological and also, to a lesser degree, biochemical methods of research. The tradition that neuropathology is mainly concerned with rendering structural elements visible by “staining” has been strong and it was often forgotten that pathology is useful to the clinician only when it explains clinical symptoms to him. Chemistry was not entirely ignored, as is exemplified by the somewhat sporadic use of histochemical methods (largely developed by workers outside the neuropathological field) and by theories, such as hysteresis (Ruzicka, 1922, von Braunmühl, 1932), tixotropie (Hallervorden, 1941) and pathocclisis (C. and O. Vogt, 1922), which did not go much beyond general applications. The consequence has been that physiological and chemical investigations have long been conducted without first-hand knowledge of the morphological data, and this has resulted, as admitted by Waelsch (1957b), in widespread and wasteful underrating of the significance of the intricate complexity of nervous tissue.* It has also led to a generation of workers using electron microscopy and other ultra-microscopic and cytochemical methods being recruited almost entirely outside the traditional neuropathological field, and it is only in the very recent past that neuropathologists have tried to make contact with these new groups.

THE CHANGING SCENE

The impact of biochemistry and biophysics is likely to transform the very fundament of neuropathology. The present writer has been greatly helped in his analysis of this process by important recent publications, which include textbooks on neurochemistry (McIlwain, 1955/59; Elliott, Page and Quastel, 1956) and Symposia of which the proceedings have been edited by Waelsch (1955, 1957a), Korey and Nurnberger (1956), Richter (1957a, 1957b) and Windle (1958).

Pope and Hess (1957) have discussed the most likely avenues of advance under the following headings:

(1) Classical microscopic histochemistry: this has, as Feigin and Wolf (1955) and Pearse (1958) pointed out, the great advantage of histological localization, but results obtained in this way are prone to artefacts and, at present, they are mainly qualitative. Nevertheless some encouraging results have been achieved in the field of enzyme-histochemistry; for instance, in specific and unspecific phosphatases (Naidoo and Pratt, 1951, 1952), cholinesterases (Koelle, 1954), dehydrogenases (Pearse). They should be appreciated, however, as a beginning only.

Perhaps, the most solid and impressive work of “classical histochemistry” has been carried out on Nissl granules. It is also work in which continuity with earlier research is particularly conspicuous. Einarson (1957) who has contributed steadily to this problem since 1932, has given an excellent survey of developments in this field. As has been already mentioned before, nucleoprotein had been suggested as the principal constituent of the Nissl bodies and nucleus before the end of the 19th century. It had also been realized, from embryological experience, that chromatin material of the nucleus is transferred through the nuclear membrane into the cytoplasm of the cell, and as early as 1899 Holmgreen reported increase of this interchange during activity. In the two decades that followed, many experimental studies were carried out to show that Nissl bodies disappeared in conditions of activity, fatigue and exhaustion

* It is interesting to learn from McIlwain (1958) that as early as 1856 Schlossberger lamented the lack of connection between histological and chemical findings.

(Dolley, 1909, 1917; Spatz 1923 among others). However, since Nissl bodies do not show the Feulgen reaction, Bielschowsky, as late as 1935 still doubted the presence of nucleo-protein. He could not be aware, at that time, that the Feulgen test (as well as methyl green) react only with desoxyribonucleic acid (D.N.A.), while ribonucleic acid (R.N.A.) is stained by pyronin. Gallocyanin, introduced by Einarson, has proved capable of giving better quantitative information than the above stains, the $(\text{CH}_3)_2\text{N}$ group of its molecule specifically uniting with nucleic acids at strong acid pH. Information, thus obtained, has been confirmed by ultraviolet microspectroscopy as well as X-ray micro-radiography (Brattgard and Hydén, 1952). Bourghardt, Hydén and Nyquist (1955) have also devised a computing microphotometer for rapid quantitative analysis.

The overall results obtained with gallocyanin and the ultramicroscopic methods of the Swedish school have been formulated by Einarson as follows: Chromo-neutrality of the Nissl bodies indicates rest or indifferent activity; moderate chromophilia may point to initial activity, while extreme chromophilia indicates suppression of activity. Moderate chromophobia is the consequence of prolonged increased activity; in extreme degree, it expresses severe stress and exhaustion. Extreme chromophobia proceeds to liquefaction of the nerve cell, whereas the outcome of extreme chromophilia is sclerosis and atrophy of the cell. R.N.A. itself which plays an important part in the synthesis of proteins is synthesized in the nucleus—under control of D.N.A. In contrast, the nucleolus is almost entirely composed of R.N.A.

(2) *Ultramicroscopes*. Ultraviolet histospectroscopy and X-ray absorption histospectroscopy, as developed by Caspersen and Hydén and their associates, has already been discussed in relation to nucleic acids. Their scope is, however, more comprehensive and they may be used for estimation of total solids, lipids and proteins other than nucleotides (Hydén, 1955). Lipochrome pigment has been extensively studied by these techniques and has been found to contain characteristic compounds of the pterin group in addition to neutral fats, chiefly cholesterol. It is also demonstrable with the periodic acid (Schiff) reaction, indicating the presence of polysaccharides. Its increase with advancing age and certain degenerative conditions is related to a corresponding decrease of cytoplasmic R.N.A. (Einarson).

Potentially, the investigations which have been undertaken in the recent past with the *electron microscope* are of profound significance (Palay and Palade, 1955; Palay, 1956; Fernandez-Moran, 1957). Electron microscopists have also devoted much attention to the Nissl bodies which Palay calls "the most impressive single architectural unit in the perikaryon". On the electronic screen it has a reticular appearance; the delicate tubules of this "endoplasmic reticulum" are lined by "Palade" granules containing proteins chiefly compounded of R.N.A. and which are the main source of basophilia. The granules are said to resemble the ergastoplasm of exocrine glandular cells and seem to be a site for continuous protein synthesis.

The nucleus contains a roseate arrangement of granules which are different from the granules lining the endoplasmic reticulum of the cytoplasm; the granules of the nucleolus are exceedingly fine. The nuclear membrane appears on the screen porous, with deep folds filled with cytoplasmic components, thus confirming that close relationship with cytoplasmic components, which had been suggested by early workers.

Among other organelles, *mitochondria* have been extensively studied. They

show, on the electron-microscopic screen, a diffuse ground substance, surrounded by a double membrane the inner lamella of which forms the characteristic "cristae", beautifully illustrated by Palay and Palade. Other workers (e.g. Belt and Pease, 1956) described "tubuli" (instead of "cristae"), but the difference seems to be one of functional degree, the "cristae" being formations at rest (Wilke, 1959). Mitochondria occur throughout the cytoplasm and extend to dendrites and axons, though, in the latter, they are less numerous. The endoplasmic reticulum also reaches into axons and dendrites.

Mitochondria seem to be particularly frequent in the vicinity of *synapses* of which three main types have been identified by the electron microscope (Fernandez-Moran). Presynaptic and postsynaptic areas are well defined by membranes and are also separated by an intersynaptic space. Thus, the neuron theory has found yet another strong support. Presynaptic terminals contain microvesicles together with numerous mitochondria. It has been suggested by Fernandez-Moran that the transfer of transmitter substances may take place through leakage into the intersynaptic space, the microvesicles constituting, as it were, small packages of one or different transmitters. Though this interesting interpretation is not yet proved, evidence may be forthcoming from electron-microscopic investigations after experimental stimulation.

The electron microscopy of *glial* cells is as yet not as detailed as that of the neuron. However, according to Palay (1958) and Hartmann (1958) all known types of glia cells can be identified and most of the older criteria of Hortega and Penfield confirmed. Apart from the shape and size of the nucleus, there are notable differences in the number of mitochondria which are consistently found in the cytoplasm of microglial cells, and are more numerous in oligodendroglia than in astrocytes (though in none of the glial varieties is the high numerical incidence in nerve cells reached). The processes of oligodendroglial cells are more delicate than those of astrocytes, but even the fibrils of the latter are not extracellular, but cytoplasmic. According to Bairati (1958), they do not contain collagen, as had been suggested by Fernandez-Moran. The processes of both astrocytes and oligodendroglia are capable of flowing movements as revealed by tissue culture. However, as Lumsden (1958) reminds us, no electron-microscopic evidence of *normal* glia is yet available.

So far, electron-microscopic research has continued mainly along morphological lines; it is now rapidly approaching a stage, however, when its results may be usefully correlated with microchemical findings and with microelectrical studies of the nerve cell (for example, those by Eccles, 1957, and his associates).

Some interesting information on the glia has been collected with the help of techniques other than electron-microscopy: tissue culture has proved to be an important instrument of investigation although all workers using this technique are aware that they are dealing with explanted tissue growing in a strange environment (Lumsden, 1958; Pope, 1958). It has, however, been possible to observe different stages of maturation. Canti, Bland and Russell (1937) were the first to observe (in vitro) mitoses in astrocytes. Oligodendroglial cells show rhythmic contraction in cycles of 5 minutes (Pomerat, 1958) which Glee (1958) interprets as indicating participation in synaptic activity (also, perhaps, suggested by the demonstration in thick Golgi preparations of boutons terminaux ending on oligodendroglia (the Scheibels, 1958)). There is fair agreement on the relative frequency of the different varieties of glial cells. In the cerebral cortex, Pope (1958) found the number of oligodendroglia and astrocytes to be almost the same while the incidence of microglia was 6–10 per cent. In the white matter, the percentage of oligodendroglia increases to two-thirds. Elliott (1958) and his

associates estimating cell density by means of D.N.A., found the respiratory rate to be low in all gliomas except in oligodendrogliomas which are, however, rather cellular tumours. These results are borne out by estimations of cytochrome activity which in astrocytomas is about half that of normal human white matter. It is interesting to be reminded by Pope that, as early as 1919, Marinesco failed to observe indophenol oxidase in glial cells. Cholinesterases and especially pseudo-cholinesterases have been brought in relation to oligodendroglia (Ord and Thompson, 1952), while carbonic anhydrase is supposed to be active in astrocytes (*vide* Pope, 1958). 5-Nucleotidase is high in white matter (Naidoo and Pratt, 1954) which also contains a larger amount of porphyrins, possibly in a zinc combination (Klüver, 1955).

It is now widely held that glial cells and particularly astrocytes which send processes to the capillaries play an important, though probably not an exclusive part in the transfer of substances from *blood to nervous parenchyma*. Wickoff and Young (1954, 1956) have stressed the intimate adhesion of astrocytic end feet to the vessel in the electron microscope, although this does not, however, prove that there is a continuous glial membrane. While Dempsey and Wislocki (1955) thought that an amorphous substance of moderate electron density filled the interspaces between capillary walls and glial cells, a more recent opinion (Dempsey and Luse, 1958; Lumsden, 1958, Pomerat, 1958 and Glees, 1958) considers the existence of a "ground substance" to be unlikely, for the simple reason that there could not be enough space for it. In favour of this ground substance Hess (1953, 1955) gave as evidence a positive Schiff reaction which seemed to develop parallel with the blood brain barrier. However, hypertrophic astrocytes also give a positive P.A.S. which is absent in young astrocytes (Lumsden, 1958; Pope, 1958).

Myelin Sheath. Striking advances have been made in this field which have led to the "wrap up" or "Swiss roll" theory of the sheath. The new interpretation may be said to have begun with the work of F. O. Schmitt and his associates (Schmitt, Bear and Clark, 1935; Schmitt, 1936; Schmitt and Bear, 1937) in polarized light and with X-ray diffraction, by which they found the myelin sheath to consist of alternate lipid-protein layers, each approximately 180Å thick and wrapped concentrically around the axon. This view was further developed by Geren and Raskind (1953), Geren (1954), Geren and Schmitt (1954) who found that at an early stage of development of chick embryo Schwann cells of the sciatic nerve envelop the axon with a double membrane contributed by the surface of axon and cell. Electron microscopy has confirmed the spiralized laminated appearance of myelin and its relation to the Schwann cell (Sjöstrand, 1953, Robertson, 1955). There is evidence that the myelin of central nerve fibres has a similar spiral appearance, but it is not yet established whether the sheath is derived from the oligodendroglia. Uzman (1958) did not find readily identifiable oligodendro-cells in the neighbourhood of areas of recent deposition of myelin, but saw only a considerable increase of mitochondria in the axons. Regeneration and myelination of axons may take place in tissue culture without the presence of Schwann cells (Glees, 1958). Costero (1958) never found excessive myelination in oligodendrogliomas, but Pomerat (1958) claims to have obtained myelin formation from oligodendro-cells *in vitro*. This problem, therefore, awaits further clarification.

(3) *Differential centrifugation.* This method, introduced by Bensley and Hoerr (1934) is based on the differing rates of velocities with which subcellular organelles tend to sediment with centrifugation. It suffers, however, from

serious shortcomings, particularly with brain tissue since the separation is only approximate and certain elements histologically easily identifiable (such as nuclei, nuclear membranes, Nissl bodies, processes) cannot with this method be identified. All these contribute to the microsome fraction which can be separated from the mitochondrial and (recently added) lysosome fraction. Nevertheless, the method has yielded information of great importance and relevance to the neuropathologist. Many important biological oxidations such as those concerned with the Krebs cycle, cytochrome oxidases, phosphorylation, enzymes governing glutamic acid and phosphate metabolism take place more or less exclusively in the mitochondria. According to Quastel (1957) snake venom lecithinase (when all other enzymes have been excluded by heat of 100° C.) has no effect on soluble enzymes of cytoplasm; its action is confined to mitochondrial enzymes, and thus affects respiratory systems. According to Harman (1958), the effect of various other agents such as bacterial toxins, diphtheria toxin, some vitamins and hormones is directed to the mitochondria. In the superior cervical ganglion cells, mitochondria show degeneration, revealed in the electron microscope, after severance of preganglionic fibres (Barton and Causey, 1958).

Earlier workers have maintained that the proteins of the brain are inert. That this view is incorrect, has already been shown by the work of Einarson and the Swedish school, centred on the Nissl bodies which are an important component of the microsome fraction. Microsome particulates have, as Waelsch (1957b) has pointed out, the shortest half-life-time, i.e. the highest rate of incorporation of labelled amino-acids such as methionine (*vide* also Gaitonde and Richter, 1955) and lysine.

There is yet only scanty information available on the lysosome fraction, as far as nervous tissue is concerned. As the name indicates, lysosomes are more related to breakdown processes in contrast to the other two fractions with their concentration on energy release and protein synthesis.

(4) *Quantitative analytical microchemistry.* The prototype of this approach has been the well-known techniques of Linderstrom-Lang and Holter who used alternate microtome sections (preferably of unfixed tissue) for microchemical investigation and histological localization respectively. The most remarkable recent advance has been made by Lowry (1954, 1957a, 1957b) who has been able to dissect by hand frozen-dried dorsal root nerve cells (0·01-0·03 γ) or Purkinje cells (0·01-0·05 γ). Samples weighing 0·005 γ or less require micromanipulator. Lowry found it practical to extend the procedure down to the size of a large mitochondrion. Among his first results he has recorded differences in amount of enzymes between cell bodies on the one side, and neuropil and myelinated fibres on the other. The cell surfaces (capsules) and the fibres contain less hexokinase, malic hydrogenase, transaminase, glutamic dehydrogenase, but are relatively rich in glucose-6-phosphate. In general, there is a striking contrast between the (low) enzyme estimates of cell bodies and the appreciably higher ones of "capsules" and fibres.

These results must, however, for the time being be received with some reserve. Lowry's ingenious procedures share with other quantitative micro-analytical methods the shortcoming that the smaller the size of the dissected cells or organelles, the less certain is the anatomical localization.

Among the structures which Lowry has investigated, is the hippocampus. He chose this centre because of its relatively simple alternate lamination of predominantly cellular and fibrous layers: i.e. for a reason similar to that which induced Spielmeyer, more than 30 years ago (1927) to use the simple cortical

architecture of Ammon's horn for his pathogenic analysis of selective vulnerability in vascular and anoxic conditions. This extensive neuropathological work, which did not remain confined to one school, was apparently not known to Lowry when he began his important studies. Nothing could better illumine the gap between traditional neuropathology and these new approaches, and the necessity for bridging it.

CONCLUSIONS

The present writer's prognosis for neuropathology is as far removed from the warnings of Cassandra as it is from complacency. It appears to him that the neuropathologist, even with his traditional techniques, will continue to be an indispensable collaborator of the clinician, whether he be neurologist, neurosurgeon or psychiatrist. His participation in the diagnosis and teaching of these disciplines will remain essential. The results of this collaboration will not be spectacular, but it will be steady work on a broad front, patiently resolving controversies, filling gaps and widening the basis of experience from anecdotal case reports to sound statistical significance. All this, however, would not be enough: neuropathology will continue to make *fundamental* contributions only in a measure as it falls into line with the basic sciences, particularly biochemistry and biophysics. This may be achieved by the neuropathologist either by acquiring additional training in the one or other basic science, according to his personal propensities, or by participation in a team. He would not enter such a team with empty hands because he has the key to a wealth of morphological data, normal and abnormal, without which the chemical or physiological approach to the nervous system would remain in a vacuum. He could become, in fact, the custodian of continuity and of a sound balance between the old and new. One cannot but agree with Waelsch that lack of this continuity (due to ignorance of each other's province) has considerably delayed progress and has been the source of misinterpretation of biochemical and physiological data. As this review of development clearly shows, this gap has been closing during the last few years, and the transformation of neuropathological thought and techniques is now in full progress.

Perhaps, to the contemporary onlooker, the present transformation appears to be more unprecedented than it actually is. The historian is able to point to earlier changes of considerable magnitude: the application of the microscope to nervous tissue in the 1830s, the substitution, from 1861 onwards, of the principle of localization for that of equipotentiality of the cerebral cortex and in the closing decades of the 19th century the introduction of precision instruments for cutting, of analytical staining methods and of greatly improved microscopes, all of which produced changes in neuropathology which, in essence and direction, are certainly comparable to those of to-day. Only the pace has immeasurably quickened and organization and communication of research has been perfected beyond expectation. It took more than 200 years from the invention of the microscope to the first major histological discoveries in the nervous system from 1830 onwards. In contrast, barely 20 years after the invention of the electron microscope in 1932, interesting and seemingly fundamental facts of nerve and glia cells, and of fibres are already extant. Electron micrographs of inorganic substances and unicellular organisms (e.g. viruses) were available at an even earlier date. The "classical" microscopists worked in isolation and for reasons which are not quite established seemed unable to disseminate the results of their work. Nowadays, particularly in the U.S.A., hardly

a month passes in which prominent scientists from all over the world do not gather to discuss problems of ultrastructure, electron microscopy, neurochemistry, neuroglia or the neurological basis of behaviour. The results of these symposia are published in monographs which, increasingly, replace the textbooks and systems of earlier and more leisurely times. They contain both new facts and new, often speculative, generalizations, and only subsequent generations may eventually be able to disentangle the facts from all their erroneous admixtures.

Today one often hears pronouncements of the end of the morphological approach in pathology. Such predictions overlook that structure and function are inextricably interlinked, and that, as a consequence, there will always be a morphological aspect of pathology. Now that the electron microscope enables us to visualize structure of molecular or near molecular size, sweeping predictions of this kind may well be confounded by new and unexpected developments.

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DRUG ADDICTION AND HABIT FORMATION— AN ATTEMPTED INTEGRATION*

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INTRODUCTION

IN view of the promise attached to the recent attempts to integrate learning and personality theory (Eysenck, 1957), and the suggestion that drug addiction might be a learned response, it would appear profitable to consider the relevance of this integration to a better understanding of addiction, a suggestion reinforced by two recent papers by Partridge (1959a, b). On the basis of a clinical survey of addiction he came to the conclusion that the extent and severity of addiction was dependent on “. . . the extent to which the particular personality can tolerate them (i.e. the symptoms, such as anxiety, which would arise without the drug) . . . patients with a low tolerance of discomforts and frustrations are those more likely to be addicts, just as they are more likely to turn to drugs in the first place . . . the development of addiction, in fact, depends much on the personality . . . the form of addiction depends more on the circumstances and opportunities with which the particular personality has been confronted.” Such considerations and conclusions can be conceptualized within and predicted from the theoretical framework to be proposed later in the present review.

Eysenck and his colleagues (1947, 1952, 1953, 1957) have demonstrated in a series of factor analytic studies, for example, that personality can be resolved into independent dimensions, and that all individuals have positions on these dimensions. The dimensions which have so far been isolated being neuroticism, introversion-extraversion, intelligence and more recently psychoticism. An independent study by Trouton and Maxwell (1956) verified the existence of two orthogonal factors of neuroticism and psychoticism. More important for the present review is that their neuroticism factor was characterized by “. . . ‘life-long or episodic anxiety’, ‘low energy output’, ‘neurotic traits in childhood’, ‘unsatisfactory adolescent adjustment’ ”. These symptoms are very characteristic of the usual descriptions of neurotic illness and there is little doubt that Partridge had just this type of person in mind when he talked about the strength of the addiction being dependent on the extent to which the individual personality could tolerate the symptoms that arose without the drug.

The second of these supposed mutually independent dimensions, introversion-extraversion, has generally received more attention, particularly in the attempts to try to place it on a causal basis. Presumably again Partridge's use of the term “personality” might tentatively be taken to include this dimension.

In the search for personality variables said to be typical of the drug addict, it is important that one of the dimensions isolated by Eysenck and his

* Based on evidence prepared for a Working Party convened by the British Psychological Society in order to present evidence to the Interdepartmental Committee on Drug Addiction.

colleagues (i.e. intelligence), does not appear to be strictly relevant to the subsequent discussion. Isbell and Fraser (1950), following a review of earlier studies on drug addiction, came to the conclusion that there was no significant relationship in intelligence between drug addicts and normals. It seems possible that, although intelligence may play a part in the genesis of addiction in the individual case, it is not a crucial factor in explaining addiction as a phenomenon.

The possibility of a relationship between addiction and psychoticism will not be pursued here since psychotic addicts are somewhat rare (Vogel, Isbell and Chapman, 1948).

Subsequent to the identification of the two main dimensions of personality attempts have been made by Eysenck to discover the causes underlying individual differences in introversion-extraversion and neuroticism. A great deal of work has been completed on attempts to place the former dimension on a causal basis.

The dynamic theory of anxiety and hysteria first presented by Eysenck in 1955 was foreshadowed by Pavlov's discussion of the methods by which experimental neurosis could be produced in men and in dogs (Pavlov, 1927, 1928, 1941). Pavlov concluded that hysterics possessed an exaggeration of the "inhibitory process" and a weakness of the "excitatory process", whilst the neurasthenic possessed an exaggeration of the excitatory and weakness of the inhibitory process. Pavlov's conclusion was next formalized in terms of Hull's psychological law of reactive inhibition by Eysenck (1955), ". . . it is easy to see what Pavlov and Hull had in mind in advocating this concept of inhibition. Whenever a stimulus-response connection is made in the central nervous system there are created both excitatory and inhibitory potentials. The algebraic sum of the potentials determines the amount of learning that takes place, and through it the particular reaction the organism makes whenever the stimulus in question is presented again."

Eysenck next proposed a postulate of individual differences with respect to the speed with which reactive inhibition was produced. This was implicit in Pavlov's own work but neglected by Hull. Following the development of a limited postulate system he argued, "The theory just outlined tells us that individuals in whom excitatory potentials are generated quickly and strongly and in whom inhibitory potentials are generated slowly and weakly, will tend to be introverted in personality. It also follows directly from our statement of the laws of excitation and inhibition that such people should form conditioned reflexes quickly and strongly. Conversely, individuals who generate weak excitatory potentials, and who generate strong inhibitory potentials tend to be extraverted in personality, such people, according to the statement of the law of inhibition and excitation should form conditioned reflexes slowly and with difficulty."

Eysenck (1957) agrees with Mowrer (1950) when he says there is considerable evidence for the proposal that, "the socialization process is mediated to a considerable extent by conditioning reactions of an autonomic kind (anxiety) and that we are immediately led to a chain of deductions which runs something like this:

- (a) Socialization is mediated by conditioning.
- (b) Extraverts condition poorly.
- (c) Introverts condition particularly well.

Therefore under conditions of equal environmental pressure we would expect extraverts to be under-socialized, introverts to be over-socialized, with people in less extreme positions on the extravert-introvert continuum showing intermediate degrees of socialization."

As a link between personality and speed of conditioning is suggested, it would appear profitable to examine the problem of addiction in the light of this (i.e. as a problem of learning) and to examine critically the theory which first gives rise to such a possible link. But first, a brief survey of some of the studies completed on the personalities and diagnoses of addicts with some reference to the possible effects of culture and environment in the development of addiction.

EXPERIMENTAL STUDIES OF ADDICTION IN RELATION TO PERSONALITY, DIAGNOSIS AND CULTURE-ENVIRONMENT

The research team at Lexington, Kentucky, one of the principal centres for research into addiction, believe that one of the most important factors predisposing to drug addiction is personality disorder (Vogel, Isbell and Chapman, 1948). It is also interesting to note at the outset of this review that the Lexington research team make a clear distinction between the more or less neurotic types of addiction and the psychopathic.

Vogel, Isbell and Chapman (1948) reviewed the personality types commonly needing treatment for drug addiction. Five general groups emerged. The first, a rather small group, consisted of patients who had received a drug for medical purposes for a long time and continued to use it long after it was required for treatment. The authors suggest an emotional basis to this perpetuation. The second group consisted of neurotics who take drugs to relieve symptoms such as anxiety. The third group (the largest) consisted of psychopaths who became addicts by associating with other addicts. A very small fourth group consisted of those who had developed addiction, the addiction obscuring an underlying psychosis. When the drug is withdrawn the psychosis becomes manifest. A final group consisted of a mixture of psychopathic and neurotic individuals who appear to make some initial attempt to adjust to society, though their adjustment is only marginal at the best of times. Addiction increases their marginal efficiency in adjustment to society.

In a later review of addiction to opiates Isbell and White (1953) said the main characteristics of this type of addict were tolerance, physical dependence ("the drug produces a metabolic state which results in a change in physical responses and the appearance of the 'abstinence syndrome' when the drug is discontinued") and emotional dependence. In a similar vein Isbell (1954) in discussing the barbiturate group, said, "... a strong physical dependence develops which necessitates an individual consuming these drugs to prevent the appearance of very characteristic illness. So they are addictive ... addiction to these particular substances (sedative or hypnotic drugs), as well as to any other drug, is more of a human problem than it is a pharmacological problem. Every addict to any of these drugs, and to any other drugs as well, always has some personality maladjustment, which, as far as can be determined from the history, anteceded the beginning of the addiction."

Henderson and Gillespie (1947) had this to say about drug addicts, "... the large number of opium habitués are people originally of a psychopathic make-up." Quoting the Mayor of New York's Committee on Drug Addiction they say that the Committee reported on 318 male cases, the majority of whom

took heroin and the remainder morphine. Half were considered to be psychopathic, and the majority of the remainder to be criminals, vagrants, homosexuals and paranoid personalities.

These results have been tentatively confirmed by the writer in an analysis of the 968 short case histories in Hathaway and Meehl (1951). These cases were a representative sample of in-patients in the Psychiatric Unit of the University of Minnesota Hospitals. Of these patients 105 were alcoholics or drug addicts. There were 77 alcoholics and 28 drug addicts. Sixty-one of the alcoholics were psychologically abnormal, showing at least one M.M.P.I. peak over 70 (i.e. 79 per cent.), whilst 19 of the 28 drug addicts (67 per cent.) returned at least one abnormally high peak. In order to obtain a finer diagnostic picture the M.M.P.I. records of the alcoholics and drug addicts were examined separately. The highest score of each patient on the M.M.P.I. was recorded. The hysteria, psychopathy and hypomania scales were considered to be the best face-validity measures of both extraversion and neuroticism—the depression and psychasthenia scales to be the best face-validity measures of introversion and neuroticism. Forty-eight of the alcoholics showed their highest peak on one of the neurotic-extravert peaks, whilst only 16 had their highest peak on the neurotic-introvert scales. Of the drug addicts, 15 showed the highest peak on the neurotic-extravert scale, only 7 on the neurotic-introvert scales.

In a review of personality studies of alcoholic addicts, Sutherland, Schroeder and Tordella (1950) summarized the results of Rorschach tests given to 383 alcoholics. The results indicated that the alcoholic lay somewhere between a neurotic and a psychopath, though the reviewers favoured a neurotic emphasis. Wilkins (1952), in making reference to this summary, said, "There are apparently two kinds of alcoholics—one looks neurotic on the Rorschach and is presumably a compulsive drinker because of neurotic personality factors. The other looks psychopathic on tests and probably in behaviour as well. The 'neurotic' alcoholic is 'self-centred, lacks emotional warmth, makes poor adjustments in his social and interpersonal situations; he is a highly constricted person, stereotyped and pedantic'". There then followed a summary of the work of Griffiths and Dimmick (1949), Halpern (1946), Kardiner and Ovesey (1951), Reitzell (1949) and Sutherland, Schroeder and Tordella (1950). According to these studies, he said, the neurotic alcoholic suffered from anxiety and guilt feelings, his principal characteristic being an inability to withstand strain and tension, meaning that he could not persevere in overcoming difficulties and disappointments in spite of high ambitions. This conclusion is similar to that of Kennedy and Fish (1959), "The addict to barbiturates is psychologically of a different make-up from the opiate addict and has more in common with the alcoholic who drinks directly to forget his troubles."

Some authors have suggested that alcoholics incline towards the introverted (Strecker *et al.*, 1939; Strecker, 1941), others have stressed the psychopathic nature of the alcoholic (Manson, 1948; Button, 1956; Landis, 1945), whilst others have sought to identify the individual at some point of the introversion-extraversion dimension (Davidoff *et al.*, 1940; Norbury, 1942; Wenger, 1944). As stressed by Franks (1958) these studies are subject to serious criticisms, especially the fact that they were based on subjective assessments. Others have failed to demonstrate differences at all between the personalities of alcoholic addicts and normals (Sutherland, Schroeder *et al.*, 1950; Diethelm, 1955; Landis, 1945; Sherfey, 1955; Jellinek, 1942; Bleuler, 1955).

Buhler and Lefever (1947) developed a series of distinguishing Rorschach signs for use with alcoholics. Such traits emerged as, "... lack of persistence in goal achievement, coupled with high ambition; lack of resourcefulness in setting up realizable goals and lack of drive to reach such goals, immaturity, anxiety and feelings of guilt; and good sense of reality."

Hewitt (1943) undertook to investigate the personality of a group of alcohol addicts, who were active members of the Fellowship of Alcoholics Anonymous (AA). Further alcoholics were later included from a city workhouse and probation office. The latter groups were selected at random. Thirty-seven members of AA were tested using the M.M.P.I. Twelve other subjects were also tested. They enjoyed drinking but rarely drank to excess. Their composite M.M.P.I. profile did not resemble the curve of the addicts. It showed only a normal deviation. Hewitt concluded, "Alcohol addiction in the group studied in this survey seemed to be associated, with but few exceptions, with deep personality disorders. Even those exceptions are doubtless more apparent than real. There were very few whose drinking was exogenously determined and whose habituation was brought about chiefly by long exposure to alcohol . . . nearly all the alcohol addicts in this study showed marked psychopathic deviation which was often associated with neurotic, paranoid, or schizoid trends." It is interesting to note Hewitt's observations on the relationship between social introversion and alcoholic addiction—"... their responses show a strong feeling of social inadequacy. A tabulation of the frequency of certain answers (M.M.P.I.) bears this out. The results suggest that many alcoholics suffer from feelings of inadequate social adjustment and inferiority which are relieved by alcohol." The nine women tested by Hewitt showed consistently greater deviation on most of the M.M.P.I. scales. He calculated that alcoholic addiction among women was indicative of a greater personality disorganization than among men. He continues, "... this may be reasonably explained on the grounds that excessive drinking meets with stronger social disapproval for women than for men, and that consequently a woman who drinks to excess might be expected to be less well adjusted to her environment . . . it is noteworthy that the psychopath deviate score of 70 is the highest of all the trait measures . . ."

Banay (1941) in a study of 102 sex offenders in Sing Sing, indicated similarly that more than half the cases showed a history of alcoholism, hostility and resentment towards authority.

Wilkins (1952), following a review of the available evidence, reaches the following conclusion, "It appears that the majority of alcoholics are basically neurotic in personality structure. On the other hand, the majority of drug addicts, at least those seen at Lexington, seem basically psychopathic." This view has also been expressed by Higgins (1953), McLaughlin and Hains (1952), Lolli (1952), Meerloo (1952), Kielholz (1952) and Knight and Prout (1951). Felix (1944), Pfeffer and Ruble (1947), Fort (1954), Gerard and Kornetsky (1954, 1955) and Isbell (1954) have all similarly stressed the psychoneurotic, psychopathic or pre-psychotic features of the drug addict. Kennedy and Fish (1959) on the other hand conclude in a review of alcoholism, that, "practically all authors agree that alcoholism is not related specifically to any one pre-alcoholic personality" (Bertagna, 1953; Williams, 1956; Wexberg, 1949; Sutherland, Schroeder and Tordella, 1950).

According to Eysenck's theory the background and circumstances which infringe on the individual will, in certain cases, be those likely to be learned. It is of importance therefore to consider briefly whether socio-cultural factors have

been shown to be relevant to addiction. The sociological studies from Yale have demonstrated a very significant relationship between the incidence of alcoholism and racial and national background (Williams and Strauss, 1950) and social status (Strauss and Winterbottom, 1949). The study of Roe and Burks (1949) of children of alcoholic parents, who had been reared in foster-homes showed that when they were reared in a satisfactory background they failed to develop symptoms of alcoholism like their parents.

Wickler (1953) has also pointed out that culture may dictate the type of drug used. Eastern cultures, it is argued, value the non-aggressive personality, thus favouring opiate addiction. The West, in contrast, favours the outgoing personality and so alcohol is approved of more and opiate addiction frowned upon. McLaughlin and Haines (1952) have demonstrated a high incidence of broken homes and a tolerant attitude to addiction, whilst Gerard and Kornetsky (1955) indicate that many addicts are truants and delinquents who drift into the illegal narcotic trade. In a cross-cultural study Horton (1943) showed that there was more drinking in "anxious" societies.

It is apparent that, apart from the agreed psychological abnormality of the addict, there is little agreement as to what constitutes the remaining major personality variables of the addict. One tentative suggestion is that, within our culture pattern, the alcoholic addict is rather more neurotic or anxious than the drug addict, the latter inclining more towards the psychopathic. The relationship between introversion-extraversion and addiction is however, on the basis of the evidence, unlikely to be a linear one. It seems opportune, therefore, to examine critically the theory which might offer a tentative explanation of the genesis of drug addiction, particularly since already there is much evidence to support the idea that drugs may alleviate those symptoms of which the individual complains and so reinforce a dependence on the drug. It will be remembered that Dollard and Miller (1950) have already pointed out that psychosomatic symptoms may be the direct physiological effect of high states of drive and an indirect product of learning whilst Masserman and Yum (1946) with cats and Conger (1947, 1951) with rats have investigated the effects of alcohol on previously learned responses. Conger demonstrated for example that alcohol reduced fear in rats and consequently reinforced the rat's response of drinking whenever it was frightened. Reichard (1947) has similarly stressed the importance of situational anxiety or anxiety arising from various somatic disorders as important in addiction. Williams (1950) and Tiebout (1951) have both postulated that anxiety is one of the major drives reduced by alcohol and so taken in times of stress, whilst Bacon (1945) and Ullman (1952) have also both stressed its tension reducing properties. Masserman's work (1940, 1943, 1946a, b) with animals supports this; whilst Stewart (1898) and Richter (1926) have shown that over-active behaviour in the rat, ascribable to tension, is reduced by alcohol. Miller (1948), in a similar vein, has shown that decreases in fear or anxiety could serve as a reinforcing agent in the learning of a habit, just as Tong (1959) has postulated that delinquent behaviour may be a learned response to anxiety which also functions as a learnable drive. Conger (1956) has suggested that conflicts produce tension, whilst Dworkin *et al.* (1937) have indicated that alcohol, amytal, nembutal and hyoscine all reduce the tension resulting from an experimental neurosis based on a conflict situation. Bailey and Miller (1952) have similarly shown that barbiturates abolished conditioned fear responses in cats and Bartholomew *et al.* (1958) that oblivon reduced anxiety in humans.

CRITICAL ASSESSMENT OF CERTAIN ASPECTS OF PERSONALITY AND
LEARNING THEORY

1. THE DIMENSIONS OF NEUROTICISM AND EXTRAVERSION

Although most studies are agreed that the alcoholic or the drug addict is poorly adjusted, there appears to be little consistency in the use of diagnostic terms. Differences are frequently drawn between the neurotic and the psychopath. In the majority of studies the neurotic appears to be characterized by anxiety, guilt, poor interpersonal relationships, etc., whilst by inference the psychopath is not neurotic though he is the asocial or antisocial individual who fails to conform to society, who is purposeless in his way of life and who does not learn from previous errors. This distinction appears to be contrary to the experimental evidence incorporated into Eysenck's explanatory theory of personality (Eysenck, 1955, 1957). According to this theory, it is the introverted neurotic who tends more to present the symptoms of anxiety, guilt, over-sensitivity to his environment and over-cautiousness. The neurotic extravert on the other hand tends to be insensitive to his environment, impulsive and unreliable. Both groups are neurotic, they differ essentially in terms of introversion-extraversion. The relationship between the dimensions of neuroticism and extraversion and diagnostic psychiatric categories has been tentatively demonstrated experimentally by Hildebrand (1953, 1958). It is the neurotic extravert who, according to Eysenck's theory, conditions or learns rather more slowly than the neurotic introvert. Differences in conditionability between these two groups are basic to his theory. As there is by no means general acceptance of Eysenck's dysthymia-hysteria dichotomy, the first essential is thus to examine critically the evidence central to this dichotomy.

Storms and Sigal (1958) have criticized the dichotomy of the extraverted-hysteric and the introverted-dysthymic. They report that Sigal *et al.* (1958) gave the Maudsley Personality Inventory to a hysteric-psychopath group and to a group of dysthymics, selected according to Eysenck's earlier descriptions of symptoms of these groups (Eysenck, 1947, 1953). The two groups were found to be significantly different on neuroticism, but not on introversion-extraversion. The hysteric-psychopath group had a mean extraversion score very similar to normals (Eysenck, 1956). The hysterics were found to be on the introverted side of normals. They quote Hildebrand (1953), Martin (1955), and Nicholls (1955) as showing results of hysterics who were also found to lie on the introverted side of normals, though not significantly so, and of hysterics who were significantly less neurotic than dysthymics. Storms and Sigal (1958) also report that, "... the MAS, the MMQ and the Guildford D+C intercorrelate most strongly, and that all three also have significant correlations with the R scale. The MMQ and the D+C scores have been used by Eysenck as measures of neuroticism and the R scale as a measure of I-E. It therefore seems quite possible that the R is loaded on neuroticism as well as on I-E (in the Hildebrand analysis, the loading was -0.25) or that neuroticism and I-E are non-orthogonal. Furthermore, not only were the hysterics significantly lower than dysthymics on the MAS (which fact Eysenck attributes to the loading on I-E), but they were also significantly lower on D+C, the best measure of neuroticism in the Hildebrand analysis."

Franks (1954) also reports large differences between dysthymics, hysterics and normals on the Taylor MAS. A significant difference occurred between the dysthymics and the hysterics. Eysenck attempts to explain this by saying, "The difference between dysthymics and hysterics is accountable for in terms of the

failure of the Taylor scale to be a pure measure of neuroticism; as mentioned before, it also has a projection on the introversion axis." It is very much to be doubted that such large differences could however be attributed to the loading on introversion, since the MMQ correlates about $+ \cdot 9$ with the MAS (Eysenck, 1957).

In a study of "Anxiety, Internalization and Eysenckian classification" (Mather and Walton, 1959), the same trend was detected. Dysthymics were more neurotic on the M.P.I. than hysterics, though this disparity did not reach statistical significance ($\cdot 2$).

Tong's demonstration (1959) that the within-hospital unstable psychopath is characterized by little anxiety in response to stressors, whilst the within-hospital "dysthymics" are characterized by too much anxiety is supportive of these trends.

Field's work (1959) also raises the question of contamination in the M.P.I. E scale. He investigated the personality dimension of extraversion-introversion with regard to a group of recidivists and apprentices. According to Eysenck's theory the criminals as a group should be more extraverted than normals when early experiences are held constant. This would be because the criminal would be less able to acquire and retain conditioned emotional needs making for socialized behaviour. Field found that the young recidivists were one-third S.D. more extraverted than the norms for the E scale, though the older recidivists were one-tenth S.D. less extraverted than the norms. He also found that the young recidivists were one-fifth S.D. less extraverted than the apprentices. He then further analysed the E scale items. He divided the 24 extraversion items into three sub-groups on the basis of their face-validity; 11 items he called social extraversion items, 7 behavioural extraversion items and 6 remaining items were termed ambiguous. In analysing the differences between the recidivists and apprentices on these three scales he found the recidivists to score significantly lower than the apprentices on nominal social extraversion—the recidivists to score significantly higher than the apprentices on nominal behavioural extraversion and no differences to be manifest on the nominally ambiguous scale between the two groups. He concludes by saying, "Whether or not the discrepancy is in self-description; that the recidivists see *themselves* as Lone Rangers, but quick on the draw; or that they want to *present* such a description of themselves; or that they really *act and live* like that, is a matter for further investigation." Field's work does lead one to consider that there may perhaps be within the M.P.I. E scale at least two types of extraversion item one of which is more subject to variation according to changes in N, that is reflecting some degree of social introversion consequent upon anxiety, the other more subject to variations according to the intensity of the other type of emotional response related to a hyper-reactive sympathetic nervous system, namely aggression. The aggressive individual would presumably score high on the total E scale, the excessively anxious person low on the total E scale.

If "hysterics" are less anxious or neurotic than dysthymics and such as Guildford's Rhythymia Scale and the M.P.I. E scale measure in part social introversion consequent upon anxiety, then these scales should reflect lower scores in dysthymics with hysterics and normals returning scores not very different from each other. This might be said to have been tentatively demonstrated by Hamilton (1959) in his summary of mean R scale scores for hysterics, dysthymics and controls (Eysenck, 1955; Franks, 1956; George, 1954; Hildebrand, 1953; Martin, 1955; Nicholls, 1955). If Tong's results (1959) are any guide, however, one would expect that psychopaths with minimal P.G.R.

responsiveness, would show on the basis of this hypothesis, the largest extraversion score, a hypothesis confirmed by Eysenck (1959). Hysterics and psychopaths combined then into one group might produce misleading results, with regard to absolute scores on the I-E continuum. Hysterics, it is hypothesized, being more neurotic (i.e. more anxious) than normals would be somewhat more introverted than them, though less introverted than dysthymics who were more anxious. Psychopaths, being the least anxious, would be the most extraverted.

In support of these ideas are Eysenck's own findings (1953) that lack of sociability and autonomic imbalance are common to both introversion and neuroticism. The fact that neuroticism and introversion may also have something in common on test evidence has been suggested by Jensen (1958). He reported high negative correlations between N and E. Eysenck (1959) recently has confirmed these trends—"In normal samples this correlation (between neuroticism and extraversion) tends to be around -0.1 , whereas in neurotic groups it rises to -0.4 . This cannot be accounted for in terms of selection. I thought at first that possibly the most neurotic and most extraverted groups might not be found in mental hospitals at all, but perhaps in prisons. However, studies with recidivist and other prison populations have shown that these have scores of both neuroticism and extraversion very similar to the scores obtained by hysterics. Furthermore, when we compared the correlations obtained from sub-groups of our normal sample, selected for high and low neuroticism respectively, we found the same phenomena, viz i.e., zero correlations for the group which is low on neuroticism and substantial negative correlations for the group high on neuroticism. These relations are definitely extra-chance; they have been found quite independently by American investigators using the M.P.I."

Certain other results are relevant. They are related to changes on testing which may occur in the acute or chronic phases of neurotic breakdown. Statistical analysis revealed (Mather and Walton, 1959) that with an increase in length of illness hysterics became significantly more neurotic ($+ .478$) and dysthymics significantly less neurotic ($- .38$) on the M.P.I. Dysthymics showed a tendency to become more extraverted and the hysterics more introverted the longer they were ill, though these changes were not statistically significant. In other words, with an increase in N in the hysterics so was there a decrease in E, and vice versa for the dysthymics, a finding predictable from the above discussion. That one must consider not only length of illness but also the age of the patient in evaluating any such differences between dysthymics and hysterics has recently been demonstrated by Nelson and Gellhorn (1958). They showed that both sympathetic and parasympathetic reactivity declined with age. This opinion has been voiced from as early as 1881 (Charcot) and more recently by Cannon (1942), Safford and Gellhorn (1945) and Andrew (1956).

Foulds and Caine (1958) have similarly observed that an extraverted or clinically hysterical type of personality may develop anxiety or a symptom more characteristic of the introverted neurotic. This they maintain may be due to the fact that the hysteric has tried to manipulate the situation and failed. It is believed that the apparent inconsistency between Foulds's findings and those of Eysenck has arisen because it has not been adequately recognized that one type of neuroticism, namely over-activity of the sympathetic nervous system, can give rise to either excessive anxiety or aggression according to circumstances, and so changes in introversion and extraversion respectively. Thus a hyper-reactor through a particular set of life experiences may be a predominantly

extraverted subject. He is nevertheless capable of generating anxiety if subject to stress. This would naturally decrease his extraversion.

Other variables which might affect the absolute scores on the N and E scales are those relating to differential response to threat and the effect of defensiveness on test scores. Alper (1946) has reported that under objectively non-stressful conditions, only those tasks which had been completed were remembered by those with weak egos, whilst those with strong egos tended to recall their failures. Under stress, however, it was the weak egos who recalled their failures and the strong egos their successes. To explain this, Eriksen (1954) has said that weak egos, threatened by the objectively non-threatening, bolster their self-esteem by recalling their successfully completed tasks. They are, however, overwhelmed by their inadequacy under stress and recall their failures. Strong egos are less easily threatened and when stress does occur they cope with it by emphasizing their successes. Low self-esteem seems to be related to a higher susceptibility to stress. Thus, it is hypothesized by Inglis (1959), that those with weak egos, whom he considers to be neurotic introverts, experience a greater degree of anxiety under ego-involving conditions than the relatively stronger egos (the neurotic extraverts) and this will disrupt effective avoidance or defensive behaviour. Rosensweig and Sarason (1942) have found also that the tendency to recall completed tasks, when self-esteem is threatened, is correlated with hysteria. Eriksen (1954) similarly found that scores on the hysteria scale (M.M.P.I.) were inversely related to the tendency to recall more incompleting rather than completed tasks when the situation was objectively self-esteem threatening. This field of work thus suggests an important hypothesis with respect to reported differences in the speed of conditioning as related to I-E to be discussed more fully in the next section. Franks (1954, 1955, 1956) has demonstrated, using a group of normal subjects, a significant relationship between I and speed of classical conditioning though not between N and speed of conditioning. If one regards a questionnaire, such as the M.P.I. as objectively non-threatening then according to Alper (1946) and Eriksen (1954) those with weak egos (presumably the marginal neurotic introverts) would be more on the defensive than the extravert. The effect on test scores would presumably be that the NI would be more likely to be defensive on neurotic items than on I-E items. Thus whilst showing a tendency towards I, they would return lower N scores than was actually the case. The marked extravert, on the other hand (with less anxiety), would be likely to manifest true lower N scores. Thus, actual scores might reflect a trend towards high E and low N and low E and low N. In other words, there might be a significant negative correlation between conditionability and extraversion and no significant correlation between conditionability and N. If, however, a low E were combined with a somewhat higher N there should then be a significant correlation between conditionability and N. Thus both N and I would be significantly related to conditionability, a fact deducible and predictable from the results contained in the present review.

On the physiological side Wenger's work (1942, 1948) supports the idea that autonomic imbalance is significantly related to neuroticism, as judged psychiatrically. Van der Meuve (1948) demonstrated that on basic emotional tension hysterics compared with normals show a shift or imbalance to parasympathetic predominance, whilst compared with normals, an anxiety group showed a shift in the direction of sympathetic predominance. Eysenck (1953) says this supports the idea of a predominance of the sympathetic and parasympathetic functions for the introvert or extravert respectively. He criticizes Wenger's work inasmuch as Wenger appears, he says, to have related sym-

pathetic predominance to neuroticism and not to have made it at all clear whether the relatively normal person is one showing a parasympathetic-cholinergic predominance. His own alternative hypothesis is that "neuroticism is correlated with deviation from autonomic balance, in either direction, while extraversion and introversion are related to the direction of the deviation from autonomic balance".

The mediating role of the autonomic in relation to the strength and persistence of conditioned drives is also clearly illustrated in the work of Solomon *et al.* (1953), Solomon and Wynne (1954), Wynne and Solomon (1955) on the effect of sympathectomies. Sympathectomies had the effect of significantly reducing "conditioned response-drive combinations".

It will be remembered that Eysenck considered that "socialization was mediated to a considerable extent by conditioning reactions of an autonomic kind (anxiety)". Tong's results (1959) indicate that different degrees of sympathetic reactivity correspond to different degrees of socialization. Those who might be deemed psychopathic showed a hyporeactive sympathetic, those who were more sociopathic (probably the "dysthymics", though including non-psychopathic aggressive subjects) exhibited considerable hyperreactivity. These differences suggest a further way in which the hysteric and the dysthymic might differ in N. The M.P.I. N scale may be overloaded with those items favouring dysthymic hyperreactivity of the sympathetic nervous system, whilst not taking sufficiently into account the postulated psychopathic hyporeactivity of the sympathetic. Hyporeactivity would appear to be just as neurotic as hyperreactivity, though at the moment a low N score might be interpreted as being more compatible with normality.

Other physiological findings of importance relate to the recording of peripheral vasomotor responses. Volume plethysmography is a method often used in estimating the peripheral blood flow in man (Barcroft and Swan, 1953). Many investigators have studied the effect of a variety of stimuli on the finger plethysmograph (Sturup, 1940; Hertzman and Dillon, 1940; Burch, Cohn and Neuman, 1942; Elithorn, Piercy and Crosskey, 1951), a method which Ackner (1956) considers the most suitable for emotionally disturbed patients, particularly in terms of simplicity and reliability of method. Only a decrease in volume was reported following a wide variety of acute stimuli. The features of these stimuli producing immediate cutaneous vasoconstriction have been the subject of much study. Ackner (1956) considers that, ". . . it appears that the vasoconstrictor response is part of an arousal or alerting reaction to a new stimulus situation. Stimuli which are emotionally significant to the individual are likely to prove more effective than those which are not so charged."

Following the pioneering plethysmographic studies of Hallion and Comte (1894, 1895) it has been recognized that excessive peripheral vasoconstriction is the product of an emotional disturbance and probably related to the sympathetic nervous system. Neumann, Cohn and Burch (1942), found an increase in pulse volume in subjects who were examined in a room more like a bedroom than when they were tested in a laboratory. Burch, Cohn and Neumann (1942) produced compatible results. Neumann, Lhamon and Cohn (1944) discovered a relationship between large pulse-waves and small finger-volume fluctuations in relaxed and contented subjects, whilst small pulse-waves and small finger-volume fluctuations were noted when anxiety was a dominant feature. Van der Meuve and Theron (1947) and Theron (1948) found that an "emotional stability-lability factor was significantly correlated with the rate of change in finger volume and that more "tense" subjects tended to show smaller pulse

volumes. Van der Meuve (1948) also demonstrated a tendency on the part of an anxiety group to have smaller pulse volumes than controls, the hysterics to have larger pulse volumes. Ackner's own experimental work (1956) confirmed that peripheral vasoconstriction was related to the anxious patient.

The tentative hypothesis emerges that those patients subject to considerable cutaneous vasoconstriction possess a hyperreactive sympathetic nervous system, that the dysthymic neurotic is so characterized though over-aggressive non-psychopathic extraverted patients are expected to respond in the same way, whereas those with a hyporeactive sympathetic nervous system should manifest peripheral vasoconstriction to a much lesser degree and be psychopathic. Hysterics might be expected to occupy an intermediate position between dysthymics and normals.

Whilst discussing the role of the autonomic nervous system and its relationship to conditioning, it must not be forgotten that in recent experimental investigations of electrical cortical activity the EEG has been used to study specifically the cortical-physiological mechanisms of the conditioned reflex (Anokhin, 1959). Anokhin made a comparative study of two types of conditioned reflex, the biologically positive (food, warmth, etc.) and the biologically negative (pain, fear, danger). As one criterion of each type of reaction he used the degree of influence exerted by the reticular formation on the cortex of the large hemispheres. A comparison of the three levels of activity of the C.N.S. (large hemispheres, thalamus, reticular formation) showed a tendency for the reticular formation to begin synchronization and desynchronization rhythms somewhat earlier than the cortex of the large hemispheres, especially in the early stages of conditioning. Anokhin argues that following Professor Dell's work it has become recognized that once adrenalin is introduced into the blood it activates the rostral part of the reticular formation of the brain stem, which in turn activates the cortex of the large hemispheres bringing about a similar desynchronization of cortical electrical activity. *It was found later that the desynchronizatory cortical conditions corresponded fully to the tension state of an experimental rabbit. Injection of chlorpromazine then eliminated the desynchronization and the conditioned avoidance response developed as a reaction against electro-cutaneous pain stimulation. Injection by adrenalin then results in clear desynchronization of electrical activity of the cortex of the large hemispheres and a heightened reaction to the previous conditioned defence stimulus.* The main conclusion from this work is that biologically negative reactions appear to develop on the basis of the integrated sympato-adrenaline system and the adrenergic mechanism of the reticular formation of the brain stem. Whilst it is thus recognized that many systems become involved in dealing with stressful situations, for the sake of clarity of exposition the role of the autonomic only will be emphasized, this step only being taken in that the evidence is very strong with regard to the similar and integrated functions of the reticular formation and autonomic nervous systems, a hyperreactive or hyporeactive sympathetic paralleled by similar degrees of arousability in the reticular formation. This viewpoint is similar to that expressed by Sigg (1959)—“Increasing importance is now being attributed to adrenergic mechanisms operating at the level of the brain stem reticular formation. Thus adrenergic neurohumors, which are highly concentrated in the brain stem stimulate the ascending as well as the descending reticular system, producing cortical activation and facilitation of motor and spiral reflex activity.”

In summary, there appears some evidence to suggest that real differences exist on the M.P.I. N scale between dysthymics and hysterics and particularly

between the dysthymics and psychopaths; that the M.P.I. E scale may be a contaminated measure (that is assessing in part changes in N according to degree of anxiety or aggression or different types of E), and that dysthymics may differ from hysterics in terms of degree of reactivity of the sympathetic nervous system. The results suggest that the dimension of neuroticism along which the normal and the neurotic occupy extreme positions (Eysenck, 1947) might be replaced by a dimension of sympathetic reactivity along which neurotics occupy the extreme positions of hypo- and hyperreactivity and normals the intermediate ones. There is less evidence available on the influence exerted by the parasympathetic in determining psychiatric differences between the dysthymics and hysterics-psychopaths. The role of the parasympathetic might be limited to its known homeostatic function. Autonomic lability and imbalance have often been said to characterize the neurotic. It is possible that such lability might occur when the parasympathetic attempts to regulate the extreme swings in sympathetic hyperreactivity and hyporeactivity. The final assessment might suggest that those with a hyperreactive sympathetic would manifest considerable anxiety in response to stress, return high M.P.I. N scores and somewhat lower E scores (scores on the part of the E scale which measures social extraversion would decrease in such cases, whilst the presence of anxiety would also undoubtedly lower the scores on the behavioural extraversion scale), whereas those with a hyporeactive sympathetic would manifest less anxiety, a lower M.P.I. N score and perhaps a corresponding increase in the E scale score.

In considering the influence of a hyperreactive sympathetic nervous system one cannot limit the discussion to anxiety. Excessive aggression can just as easily arise from an over-active sympathetic, providing the circumstances are suitable (one of the most important of these is that the subject has not previously been the centre of too many "anxiety" situations). Thus the additional suggestion is made that the separate behavioural E scale existing within the total M.P.I. E scale might reflect differences in the degree of aggression developed as a result of sympathetic over-activity. It is not considered, however, that this scale is entirely independent of "social extraversion" which might well reflect variations in anxiety. The aggressive individual might be less anxious (subject to the above qualifications) and so return moderately high social extraversion scores. In a similar way the anxious person might be said to be less impulsive than the aggressive person and so returns somewhat lower behavioural extraversion scores. Thus an over-active sympathetic might be responsible for either excessive anxiety or aggression, these related to introversion and extraversion respectively.

2. SPEED OF CONDITIONING

The first prediction made by Eysenck on the basis of his theory related to the establishment of conditioned responses. The evidence available on this point can be subsumed under the following three headings (a) experimental, (b) clinical-experimental, (c) symptomatology.

(a) *Experimental*

The first crucial experiments were carried out by Franks (1954, 1955, 1956) —"It was found that dysthymic neurotics formed conditioned reflexes very easily and that these reflexes were difficult to extinguish, whereas hysterics and psychopaths formed conditioned reflexes very poorly, and that, once formed, these reflexes were readily extinguished. It was found also that intro-

verted normal subjects conditioned much better than extraverted normal subjects. For all groups there was a significant correlation between conditionability and a personality questionnaire which measured introversion-extraversion, and there were no significant correlations between conditionability and questionnaires which measured the dimension of neuroticism. These findings strongly suggest that the underlying causal explanation for the personality dimension of introversion-extraversion is indeed to be found in the cortical processes of excitation and inhibition as adumbrated by Pavlov."

Franks did, however, add cautiously, "... drive does not affect conditioning in situations where the drive is an irrelevant one . . . it is, for example, clear that drives may increase the learning of instrumental responses (Munn, 1950), but it would seem difficult to conceive of eyelid conditioning in the present series of experiments as primarily and consistently instrumental. It is also clear that under certain circumstances, drives increase conditioning when the drives are directly relevant to the conditioned stimuli, thus Zener and McCurdy (1939) found that hungry dogs yield a greater conditioned salivary response than non-hungry dogs, and Lashley (1916) and Winsor (1928) obtained similar results with humans.

Franks (1957) conducted a further experiment to test the Spence (1951, 1953), Taylor (1951, 1956) and Hull (1943, 1950) prediction that increased drive strength increased conditionability and that, "total effective drive . . . is determined by the summation of all extant need states, primary and secondary, irrespective of their source and their relevancy to the type of reinforcement employed". His results failed to demonstrate support for the Spence-Hull theory of conditioning, although he concluded that the results were in agreement with an alternative theory which related conditionability to introversion-extraversion and that drives do not summate in the way suggested by Hull. In this experiment a conditioned eyeblink response was developed at the same time as the subject was suffering from food, drink and tobacco deprivation.

In summary, Frank's work suggests that in an experimental situation involving classical conditioning, speed of conditioning may be related to the I-E dimension and not to neuroticism, though not denying the relevance of instrumental learning in other contexts which might operate with either neuroticism or anxiety as the drive.

There is by no means agreement on this subject. Storms and Sigal (1958) have criticized Eysenck's inference that "conditionability" was a unitary trait, quoting in support of their argument the work of Razran (1939) and Roff, Payne and Moore (1954). They make other criticisms of Frank's experiments. They ask whether the groups were equated on initial sensitivity to the tone? They argue that the supposed superiority of the dysthymics over the hysterics in the total number of blinks was due to higher spontaneous blink rates among the dysthymics. They also added that the high negative correlations reported between extraversion and conditionability may be inflated because the subjects chosen for the experiment were extreme scorers on extraversion or introversion. Eysenck (1959) answered some of these criticisms. He argued, for example, that the available evidence did not suggest a positive relationship between blink scores and data from personality inventories (Meyer, Bahrnick and Fitts, 1953), whilst Franks (1956) did not find any significant differences between hysterics and dysthymics over a one-minute period following the conditioning and extinction trials. He added that this would load the dice in favour of Storms and Sigal because of the possible reminiscence effects.

Such authorities as Hilgard, Hull and Skinner are also not agreed about the

independence of classical Pavlovian conditioning and instrumental learning. Hilgard, for example, says there is no clear evidence for the Pavlov type of conditioning, depending, as it does, on the approximate simultaneity of stimuli. Skinner (1938) also does not believe it exists in such a pure form. Skinner favours instrumental conditioning, that is reinforcement cannot follow unless the conditioned response appears.

Hilgard similarly presents evidence to the effect that when the experimental circumstances are excellent for demonstrating type S conditioning (Pavlov classical), it is very difficult to demonstrate conditioning (Wedell, Taylor and Skolnick, 1940; Hilgard, Dutton and Helmick, 1949; Young, 1954). On the other hand Kotake and Mihama (1951) and Mihama and Kotake (1954) have reported success, though their results were highly unstable.

Examination of the available evidence does not suggest with any degree of confidence that classical conditioning exists in such a pure form as suggested by Franks. Part at least of the results might alternatively be explained on the grounds of instrumental learning. The puff of air might, for example, be regarded as a stressful stimulus. To this stimulus those with a hyperreactive sympathetic nervous system will generate considerable anxiety. The blink will reduce this stressful anxiety, thus the more anxious the patient the greater the need to reduce this unpleasant feeling. It will be remembered that many of the studies conducted previously with regard to pain threshold demonstrated an over-reactivity to pain stimulation in neurotics (Hall, 1953; Lanier, 1943; Chapman and Jones, 1944; Clausen and King, 1950; Rez, 1943; Wolff and Goodell, 1943; Chapman, Finesinger, Jones and Cobb, 1947; Hemphill, Hall and Crookes, 1952; Chapman, Cohn and Cobb, 1946; Malmö *et al.*, 1948; Malmö and Shagass, 1949; Malmö, Shagass and Heslam, 1951; Malmö and Shagass, 1952). Tong's work has also demonstrated, in this context, that people showing hyperreactive autonomic nervous systems and high autonomic conditionability also show a rapid report of pain. They tolerate it far less. Thus, following a rapid build up of anxiety in the hyperreactors (both as a reaction to an experimental stressor and to the laboratory (Neumann, Cohn and Burch, 1942)) there is an increased drive towards a reduction of this anxiety as soon as possible. The subject therefore blinks as soon as he hears the tone because the tone has always preceded the puff of air, and the blink is an effective unconditioned avoidance response. The model seems to be precisely the same as that operative with Tong's patients. Those patients who tend to report pain later show a lower conditionability score and extreme inhibition with regard to stress reactivity. They are less easily aroused in other words and so instrumental learning is required to a lesser degree.

It will be remembered that hyperreactivity can result in either excessive anxiety or aggression and that they might be related to introversion and extraversion respectively. Tong apparently demonstrated, however, that as both groups could not tolerate stress they both conditioned quickly. Thus a NE might not necessarily have a bad prognosis because anxiety can be generated. Eysenck would however consider the NE to have an unfavourable prognosis because of the poorer conditionability of the extravert. Tong's work thus provides an apparent contradiction to Eysenck's theory inasmuch as a small group of discharged hyperreactive patients showed a tendency towards subsequent social stability, irrespective of temperament. It was the hyporeactive subject who showed a lesser tendency towards improvement. Socialization might therefore be conceptualized within an instrumental learning model with emotionality acting as the drive.

Additional hesitancy with regard to accepting Franks's results might be suggested by the hypothesis developed in the previous section following an examination of the findings of Alper (1946) and Eriksen (1954). Both workers suggested that when the person with a weak ego (NI) was confronted by an objectively non-stressful stimulus he would tend to be on the defensive. It was argued that if this hypothesis was correct, then Frank's results were inevitable, though not necessarily correct. The result to be expected, if defensiveness were not present, would be significant correlations between speed of conditionability and both N and I. This result would be consistent with the results of the many researches reported in this paper and predictable from them.

That caution should be observed before accepting Frank's suggestion of a significant relationship between conditionability and introversion is thus reinforced by the results of the various quoted studies. It is felt, at this stage of the review, that studies still need to be conducted to establish much more adequately the degree of conditionability as related to I-E and indeed to establish whether there is such a thing as classical conditioning which is emphasized in the introvert and which is shown to be independent of the influence of one aspect of N (anxiety).

(b) *Clinical-Experimental*

Evidence that conditioning and introversion might be related was provided by the findings of Franks and Laverty (1955), Laverty and Franks (1956) and Laverty (1958) that sodium amytal, a cortical depressant, reduced conditionability and at the same time increased the degree of extraversion. The work of Shagass (1954, 1956, 1957) and Shagass and Naiman (1955, 1956) is relevant. Eysenck continues, "... Sodium amytal, being a depressant drug, would be postulated to increase inhibition. An extravert, whose cortex, according to our theory, is already in a relatively inhibited state, should require comparatively little sodium amytal before reaching the critical sedation point; such a person should have a low sedation threshold. The introvert, on the other hand, whose cortex is in a state of considerable excitation and low inhibition, would require a considerable amount of sodium amytal before reaching the critical sedation point; he would be predicted to have a high sedation threshold. If we express this general hypothesis in terms of neurotic groups and their standing on the extraversion-introversion continuum, then we would expect psychopaths to have the lowest threshold, followed by the hysterics. Mixed neurotics would be intermediate and anxiety states, obsessionals, and reactive depressives would have high sedation thresholds." Shagass's results tend to bear out these predictions, though one must bear in mind not only that recently serious criticisms have been levelled at his criteria of sedation (Ackner and Pampiglione, 1959) but that the reported differences might alternatively be due not directly to differences in I-E, but to differences in the degree of reactivity of the sympathetic nervous system. His results show some support for this. There is one crucial omission in his experimental population. No psychopaths were included in his different neurotic groups. From the previous discussion it will be apparent that two classes of patients might psychiatrically be classified as psychopathic and indeed perhaps manifest very similar aggressive behaviour. They would be the hyper- and the hypo-reactors. The hyperreactor would, in the laboratory-type situation necessary for the assessment of the sedation threshold generate considerable anxiety. *His sedation threshold would be expected to be high, though on testing he might well be extraverted because of considerations discussed*

previously. On the other hand the hyporeactor will generate little anxiety and so manifest a low sedation threshold. He might also be expected to be extraverted. Differences in sedation threshold might therefore be explainable on the grounds of differences in sympathetic reactivity rather than I-E, though because of the close incidental relationship between these two variables apparent agreement between Shagass and Eysenck would be expected.

Individual differences in alcohol tolerance in humans may be related to these results (Victor and Adams, 1953), as might Drew's work (1958) on the relationship between driving skills, alcohol and extraversion. Mayerhoffer (1933), Vernon (1936), De Silva (1937) and Newman (1955) have all similarly demonstrated the deleterious effects of alcohol on the learning of driving skills. In this context it will be remembered that Eysenck (1947) found that extraverts ascribed the characteristic of "accident proneness" to themselves more than did the introverts. Kerr (1950) and Kral (1953) produced similar results. Kerr administered the Bernreuter Personality Inventory Scale to accident and non-accident cases. He found that the accident cases were *less neurotic and less introverted* (a finding of interest especially in view of previous discussion), more self-confident and returned higher dominance scores. Kral selected from hospital records 32 accident repeating children and matched them with a control group for age, mental age, sex, school and grade. Two 20-minute standardized doll play interviews were carried out. The accident-prone children showed more aggression in their doll play, less inhibition, less delay in expressing aggression, more activity and more commands, threats and prohibitions in their doll play. In other words accident-prone individuals show a tendency towards extraversion and less anxiety than non-accident-prone subjects. One might say that anxiety produces caution and so less risk of accidents. The anxious introvert would therefore tend not to have accidents and would require correspondingly more alcohol than a less anxious person to reduce his anxiety level to the point where carelessness would arise.

At first glance one might say that these results appear in a general way to be supportive of Eysenck's personality-drug action postulates and predictable from them. In his chapter on drugs and personality Eysenck (1957) provides further evidence and many references to work and results which he considers deducible from his general theory. There are five major references dealing with attempts to relate drug-action and personality to the effects of continuous work, visual after-effects, etc. These experiments on the whole are again superficially supportive of his general hypothesis of a relationship between drug-action and personality (Eysenck, 1957).

Further clinical-experimental evidence can be and has been adduced in support of his general theory. Kennedy (1954, 1955) has pointed out the similarities between the hysteric, the psychopath and the brain-injured person. Experimental support for this opinion is provided by the work of Petrie (1952, 1953, 1956), Le Beau (1954), Le Beau and Petrie (1956) and Teuber and Weinstein (1956). A full discussion on the relationship between brain-damaged and extraverted behaviour is contained in Eysenck (1952). More important for the general argument is that Reese *et al.* (1953), Gantt (1950) and Gantt *et al.* (1942) have shown a lack of conditionability to follow brain damage. Similarly Klein and Krech (1952) have demonstrated that the brain-injured show greater figural after-effects than the non-brain-damaged. The hysterics showed very similar results to the brain-injured. Skinner and Heron (1937) also report the restoration by amphetamine of conditioned reflexes, in rats, which had been extinguished, whilst Lewis's (1947) work suggests that those who have received

head injuries are more susceptible to the effects of alcohol and the shorter the interval between the head injury and the alcoholic addiction the greater the likelihood of abnormal anti-social behaviour. Several earlier studies also apparently support Eysenck's proposals. Shorvon (1945), Hill (1947) and Shorvon (1947) all describe the successful application of benzedrine to the treatment of psychopathic states and behaviour disorders. Bradley (1937), Bradley and Bowen (1941) and Lindsley and Henry (1942) compared the beneficial effects of benzedrine with those of barbiturates which tended to exacerbate the symptoms of this group. Hill and Waterson (1942) and Hill (1944) observed the presence of an abnormal EEG in certain adult cases of psychopathy, associated with aggressiveness in the personality. Success was achieved with amphetamine sulphate with these patients.

Shapiro (1951, 1952, 1953, 1954), basing his work on Pavlov's negative induction model, also carried out experiments using brain-injured and non-brain-injured patients. Negative induction ("excitation of one part of a sensory surface leads to inhibition in other parts"), was found to be much stronger in the former group. It is difficult to decide at the present state of knowledge on the extent to which reactive inhibition, satiation phenomenon and negative induction are the same. Shapiro's results appear nevertheless to offer many interesting leads which do not appear unrelated to the general theoretical formulations above.

Further clinical-experimental evidence concerning the validity of Eysenck's proposals comes from the application of principles directly deducible from his integration of learning and personality theory to the treatment of clinical problems. According to this theory the introverted neurotic should respond to conditioning types of treatment, the extraverted neurotic to inhibitory types of treatment. Jones (1956) and Walton (1959a, b, c, d) successfully applied conditioning techniques to the treatment of introverted neurotics, whilst Yates (1957) and Walton and Black (1959), working with extraverted patients, successfully made use of reinforcement by inhibition. Meyer (1957) and Walton and Black (1959) similarly successfully treated patients by stimulant and depressant drugs, the drugs being used according to Eysenck's drug-action postulates.

Although Lavery (1958) has demonstrated an increase in extraversion following the administration of sodium amytal, *he has also demonstrated a reduction in neurotic symptoms such as anxiety, depression, obsessional thoughts, etc.* This reduction occurred more frequently in the neurotic introverts, though it was by no means exclusive to them. To measure extraversion he used Guildford's rathymia scale (Guildford, 1940). Franks (1957) has, however, criticized this scale because certain of its items correlate more highly with the total score on the C and D scales, i.e. those characterizing neuroticism, than with the total score on the R scale. It leads one to suggest nevertheless that an increase in E might sometimes be associated with a decrease in N. Results similar to those of Lavery have been reported by Petrie (1952). Following leucotomy she found both a decrease in neuroticism and an increase in extraversion. This type of response has also been observed in a clinical-experimental study by Walton and Black (1959). Following improvement in a case of chronic hysterical aphonia there was a significant drop in neuroticism and a most significant increase in extraversion. The fact that Franks and Lavery (1955) demonstrated a reduction in conditionability and an increase in extraversion following the administration of sodium amytal links up very well with the results of these other studies. If anxiety is reduced by amytal with the result that

extraversion scores increase, and if instrumental learning does play a part in Franks's experimental work, as has been suggested, then conditionability should also be lowered in the extravert. The central role of anxiety and tension in the development of conditioned reflexes was illustrated forcibly by Skinner and Heron (1937). Activation of the sympathetic nervous system by amphetamine restored previously extinguished conditioned responses. The administration of sympathomimetic amines, e.g. amphetamines, by Shorvon (1945), Hill (1947), Shorvon (1947), Bradley (1937), Bradley and Bowen (1941) and Lindsley and Henry (1942) to the treatment of psychopathic states is relevant. Improvement in behaviour might well have occurred because of the increased arousability of the sympathetic nervous system. Anokhin's results (1959) are fully consistent with this interpretation. In addition, if Laverty's article (1958) is any guide there is a significant increase in distractibility following the administration of sodium amytal, an effect also designed to lower the conditionability of the patient.

There is much in this section which people might regard as supportive of Eysenck. It appears that there might be a relationship between drug-action and personality. Both experimental and clinical studies tentatively suggest this. It is, however, in the interpretation of this relationship with respect to speed of conditioning and personality that difficulties arise. An alternative interpretation to that provided by Eysenck is suggested.

(c) *Symptomatology*

A final piece of evidence should be provided, according to Eysenck, by the theory being able to account for the dominant features of the hysteric and the dysthymic repeatedly described in psychiatric textbooks. In Eysenck (1957) an attempt is made to effect a link between excitation-inhibition and the usual clinical personality descriptions of the hysteric and the dysthymic. The main distinction drawn between the two groups is the failure of the former group to become as socialized as the latter. Two sets of evidence are reported early in his chapter on socialization and personality—the experimentally observed facts relating to hysterics and to dysthymics and secondly the predominant clinical features of these groups (Henderson, 1939; Maudsley, 1896; Kahn, 1931; Bianchi, 1906; Sadler, 1936; Bumke, 1948; Delgado, 1953; Henderson and Gillespie, 1947). The differences which had been demonstrated experimentally between hysterics and dysthymics were in intellectual functioning (Himmelweit, 1945; Foulds, 1956), persistence (Eysenck, 1947), speed/accuracy ratio (Himmelweit, 1946), level of aspiration (Himmelweit, 1947; Miller, 1948), sense of humour (Eysenck, 1947, 1956), social attitudes (Eysenck, 1954) and qualitative performance on the Porteus Maze Test (Hildebrand, 1953; Foulds, 1951). These experiments all again tend to support the hypothesis of the dysthymic's over-socialization compared with the hysteric, though not necessarily for the same reasons as advanced by Eysenck.

It will be remembered that Eysenck's argument is as follows. As both the hysteric and the dysthymic are fundamentally the same in neuroticism an elucidation of the ways in which they differ is basic, i.e. in those characteristics related to extraversion-introversion. He considered that he had to explain in terms of his theory, the following points:

1. "The failure of socialization in the hysterico-psychopathic group as compared with the dysthymics.
2. The development of anxiety in relation to neutral stimuli on the part of the dysthymics, as compared with the hysterico-psychopathic group."

Having made the hypothesis that the socialization process was mediated to a considerable extent by conditioning reactions of an autonomic kind (anxiety), he went on to suggest, on the basis of his previous experimental work, that,

- (a) "Socialization was mediated by conditioning.
- (b) Extraverts condition poorly.
- (c) Introverts condition particularly well.

Therefore under conditions of equal environmental pressure we would expect extraverts to be under-socialized, introverts to be over-socialized, with people in less extreme positions on the extravert-introvert continuum showing intermediate degrees of socialization."

He continued,

"The individual's failure to condition easily, on this view, accounts for his failure to become fundamentally socialized, and thus is responsible for those many-sided behaviour patterns. This would appear to be a truly dynamic account of the genesis of hysterical, psychopathic and criminal behaviour patterns . . . precisely the opposite picture is predicted, and found, among introverts and dysthymics. Here we have, in the ethical realm, an excess of socialization leading to pre-occupation with social duties, ethics, guilt and similar moral notions . . . the theory accounts also for the main features of dysthymics' personalities, namely their excessive anxiety reactions. Strong autonomic-emotional lability and reactivity produce excessive fear reactions to painful and harmful stimuli; through unusually strong and responsive conditioning mechanisms these fear reactions become attached to accidental, irrelevant, neutral stimuli which happen to precede or accompany the fear producing occasion. Through their connection with these conditioned fears or anxieties, the previously neutral stimuli now acquire drive properties, such that avoidance of these stimuli became rewarding through reduction of the conditioned fear or anxiety attaching to them . . . the fears and anxieties of the dysthymics are the products of excessively high drive and excessively high conditionability ($D \times S R$)."

In a similar vein Franks (1956) has this to say about recidivists, "One could predict that those recidivists who were introverted in personality, and who also conditioned well would be the ones whose environment had been a continually undesirable one, and with whom no serious attempts at re-education or psychotherapy had been made. This kind of recidivist would probably respond favourably to such attempts and in particular to thorough attempts to condition him to a more desirable form of environment. On the other hand, one could predict that those recidivists who were extraverted in personality, and who formed conditioned reflexes very poorly and whose conditioned reflexes were soon extinguished would be the ones who should be classed as psychopathic. Such recidivists, possessing a constitutional excess of cortical inhibition, would be constitutionally unable to learn (i.e. condition to) the rules of the society in which they lived, no matter how socially perfect their environment. This kind of psychopathic recidivist would probably fail utterly to respond to re-education or psychotherapy."

Several studies are relevant to these formulations and again at first appear to support Eysenck and Franks. Marcus (1955) studied a large group of prisoners who had passed through H.M. Prison, Wakefield. Recidivism was found to be largely associated with introversion. Those prisoners who tended to get into trouble after release tended to be extraverted in personality. Franks deduces, "It would seem reasonable to postulate that the majority of so-called 'recidivists' tend to be slightly introverted in personality; these people have simply fallen into a criminal environment, they are amenable to training and are not intrinsically psychopathic. On the other hand, there is a small proportion of recidivists who tend to be more extraverted in personality; these people are in general not amenable to training and would probably be best classified as psychopathic."

Tong and Mackay's (1959) work tends to support this viewpoint. They found, in a statistical follow-up of mental defectives of dangerous or violent propensities, that the type of behaviour in hospital associated with relapse, following transfer from Rampton, was characterized by aggression, escaping, attempting to escape, and possibly damage (i.e. under-socialized relapses). They also found that length of stay was related to a good prognosis. They found that the mean length of stay was much less for the relapse groups than for the other groups. This is consistent with Eysenck (1959), "... I have shown how psychopathic reactions originate because of the inability of the psychopath, due to his low level of conditionability, to acquire the proper socialized responses. But this failure is not absolute; he conditions much less quickly and strongly than others, but he does condition."

Field (1959) has similarly found that when two groups of prison inmates are compared, those that were in prison longer were significantly more neurotic and more introverted. Both groups were more neurotic than normals, but only those that had had a lot of past prison experience were less extraverted than normals. The young recidivists were one-third S.D. more extraverted than the norms. Although he has not yet been able to quantify the data, it appears from the case histories that more of the older recidivists endured "abnormal or abnormally weak pressures to conform in early life".

Durand (1955), in a prognostic study, provided evidence compatible with the formulations of Franks, Tong and Eysenck. He divided his patients into two main groups, the compulsive and the impulsive. The impulsive felt no regret or guilt over their addiction whilst the compulsive addicts felt that their condition was wrong. After three years 1 of the 33 impulsive addicts had recovered (approximately 3 per cent.), whilst 4 of the 22 compulsive addicts (approximately 20 per cent.) had recovered.

Hansen and Teilman (1954) investigated a group of convicted criminal alcoholics. They were divided into two groups. The first group were abnormal psychologically and long-term prisoners, the second group were under short-term detention orders and soon released on parole. The former group had a substantial number with head injuries (possibly more extraverted). Only 13 per cent. of this group improved, in spite of therapy, whereas 35 per cent. of the other group improved without treatment.

Thus, although this section contains studies which provide apparent support for Eysenck's theory the results also suggest an alternative explanation, as have the previous sections. First, Eysenck considers that there are two types of activities which each person has to learn. The first of these can be subsumed under instrumental conditioning, the second under classical Pavlovian conditioning. In illustrating the latter, he suggests that the expression of aggressive and sexual urges, for example, may be rewarding in themselves and so instrumental conditioning and the law of effect are not relevant and that the satisfaction of these urges therefore without regard to the consequences should be effected very easily. It might well be argued alternatively that this is an example of instrumental learning. A person may experience sexual feelings but because of anxiety and fear of rebuff, etc. he does not translate these feelings into overt behaviour. His failure to make sexual advances therefore avoids the possibility of rebuff and anxiety, and so is instrumental in creating and reinforcing what is a respectable social response, that is a lack of response. In the same way and for similar reasons people may learn to refrain from other types of anti-social behaviour. A neurotic introverted boy by associating with "bad lads" can develop a delinquent style of behaviour. Eysenck might argue

that this is due to the marked conditionability of this type of person. An alternative explanation might be as follows. His delinquent friends represent sources of stress in that failure to follow their style of behaviour might result in criticism which the boy cannot tolerate. Conformity therefore reduces this anxiety and is responsible for the development of his delinquency.

Tong (1959), in a series of laboratory studies with psychopathic defectives, demonstrated that reactivity to stress varied from a high degree of excitation (much anxiety) to one of a high degree of inhibition (little anxiety). Subjects who were rated as unstable within the hospital were found to be of either a very high stress reactivity or very low reactivity. Stable subjects within hospital demonstrated a moderate degree of reactivity. Patients who demonstrated a subsequent social instability following discharge from hospital showed a tendency to manifest low stress reactivity. High stress reactivity was associated with subsequent social stability following discharge. Although there are similarities between these results and Eysenck's ideas, an alternative explanation can be offered to his own theory. Eysenck suggests that since the dysthymics and the hysterics are similar in terms of neuroticism, differences in socialization are due to differences in I-E. Any anxiety which is aroused in the dysthymic becomes attached to irrelevant stimuli because of the greater conditionability of this type of patient. In the hysteric poorer conditionability therefore fails to relate this anxiety to these stimuli. Tong's work appears to contradict this for many of his under-socialized psychopaths were hyporeactive on tests of sympathetic reactivity. They failed to register much anxiety. Their under-socialization may in part be therefore attributable to an absence of fear of consequence or a poor arousal to the possible stresses associated with anti-social behaviour rather than due to poor conditionability dependent on extraversion. Those psychopaths who showed subsequent social stability were hyperreactors, that is they were capable of generating excessive anxiety responses, even though their behaviour might show signs of impulsiveness and extraversion.

One inference from Field's work, especially in view of the previous discussion, is that although the longer term inmate may score lower than the norms on I, the older recidivists are nevertheless showing response to treatment. This might be formulated in another way. The older recidivists when first committed to prison exhibited aggressive anti-social behaviour. The fact that on test evidence they now return high neuroticism scores might indicate that their aggression was originally the result of a combination of adverse environmental pressure and a hyperreactive sympathetic nervous system. They might therefore have exhibited on admission, if testing had been carried out, a picture very similar to the young recidivists in Field's study, that is somewhat more extraverted in behaviour. As has been stressed in this paper hyperreactive aggressive subjects are capable of generating excessive anxiety responses, though their speed of response to treatment, dependent on this anxiety, might vary according to the rigidity of the aggressive behaviour pattern developed as a result of years of unsuitable environmental stimulation. Thus the hyperreactive aggressive criminal would respond to treatment though only slowly, this depending on the degree of rigidity. As he improved he would thus become less extraverted. This is of course not saying that he is responding to treatment because he is introverted, *it is rather suggesting that NE can respond to treatment providing they are hyperreactors.*

With regard to Marcus's results (1955), he found that those prisoners who tended to get into trouble after release tended to be extraverted in personality.

Several times in this review results have been quoted showing significant negative correlations between extraversion and neuroticism and which suggest that the M.P.I. neuroticism scale may be more a measure of sympathetic N.S. over-reactivity. If this is the case then those extraverted inmates who relapsed may either be less anxious (the hyporeactors) and so motivated less towards social conformity, i.e. the true psychopath, or hyperreactors who had been subject for too long, before prison committal, to adverse environmental pressure so that they find it extremely difficult to change the rigidity of their aggressive behaviour pattern.

In Eysenck (1957) further examples are given of human classical conditioning—"In the experiment the subject may be shown a series of words on a screen. Every time a particular word is shown to him an electric shock is administered. Very soon the psycho-galvanic reflex which always accompanies the shock becomes associated with the word itself, which thus becomes a conditioned stimulus." By experiments similar to this Eysenck has tried to demonstrate a relationship between I-E and speed of classical conditioning. This experimental design might also be considered instrumental rather than classical in its emphasis on the type of learning demanded and so raise further doubts about a significant relationship between I-E and conditionability of the Pavlovian type. It might be argued that the establishment of a relationship between the presentation of a word and an exaggerated P.G.R. response is evidence of an arousal response on the part of the patient, preparation for the reception of a noxious stimulus, i.e. bodily preparation to meet something unpleasant and so indirectly rewarding. It helps to meet the threat. If the sympathetic is less easily aroused, less *additional* sympathetic activity may be in evidence, and much less relationship between a word and a P.G.R. response would thus be demonstrable.

CONCLUSIONS AND SUGGESTIONS ARISING OUT OF THE CRITICAL ASSESSMENT OF CERTAIN ASPECTS OF PERSONALITY AND LEARNING THEORY

1. *Evidence Related to the Validity of Eysenck's Dysthymia-hysteria Dichotomy*

The evidence suggests:

(a) That real differences exist on the M.P.I. N scale between dysthymics and hysterics.

(b) That the dysthymics and hysterics differ in the degree of sympathetic reactivity.

(c) That reported differences between these two groups on the M.P.I. scale may be partly due to this scale being more a measure of sympathetic hyper-reactivity.

(d) That it is possible for those patients showing a hyperreactive sympathetic nervous system to manifest either considerable anxiety, high M.P.I. N scores and somewhat lower M.P.I. E scores (scores on the social extraversion scale would decrease in such cases), or considerable aggression with a corresponding increase in E. Because the N scale appears to favour anxiety-type items the neurotic aggressive hyperreactor might return spuriously low N scores. Those patients with a hyporeactive sympathetic nervous system might manifest correspondingly lower N scores. Since the hyporeactor generates little anxiety and conditions badly (Tong, 1959) it is suggested that the term psychopath might justifiably be restricted to this diagnostic group.

(e) That the M.P.I. E scale may be a contaminated measure, that is measuring in part N and different types of E, a decrease in E associated with anxiety, an increase in E associated with the presence of aggression.

(f) That if one wishes to retain the term neuroticism for both the dysthymics and the hysterics, then abnormality might be understood in terms of the former's tendency towards hyperreactivity, somewhat less reactivity in the hysteric, with the psychopath showing a tendency towards hyporeactivity in his sympathetic nervous system. All three groups might be considered to be neurotic, the former because of an excessive emotional response to stress, the latter because of a hyporeactive emotional response.

(g) That circumstances and experiences are important determinants in the behaviour of the hyperreactors, of much less importance in the hyporeactors.

2. Evidence Related to Speed of Conditioning and Personality

Because of the probable contamination of the M.P.I. E scale and because of its relationship to the N scale, it is possible that Franks's results reflect the influence of instrumental learning in which anxiety acts as the drive. A suggestion arising from the work of Tong and Field might be that the over-socialization of the dysthymic is due to excess anxiety, this in some instances acting as the drive, in others disrupting effective social behaviour so that unreasonable degrees of conformity result, whilst the relative under-socialization of the hysteric-psychopath is attributable to the presence of a lesser degree of anxiety. The evidence which attempts to relate degree of socialization to differences in I-E is much less convincing. Tong's work (1959) in this sphere is basic. A fundamental difference between Eysenck and Tong relates to the committal of anti-social acts by neurotic introverts. Eysenck would suggest that those NI with anti-social histories turned to crime because of their greater conditionability dependent on introversion and because they were also subject to anti-social backgrounds. Nevertheless these people would respond to therapy. Tong has shown, however, that people with a hyper-reactive sympathetic nervous system (i.e. *people with excessive anxiety (introverted) or aggression (extraverted) show, following treatment, a tendency towards social stability*). It is only when there is an absence of anxiety or responsiveness that the patient fails to respond to treatment.

Much of the evidence relating speed of classical conditioning and introversion thus remains equivocal, though a strong positive alternative explanation links socialization with instrumental learning dependent on anxiety.

3. Suggested Amendment to Eysenck's Theory

If Eysenck wishes to regard dysthymics and hysterics as similar in terms of neuroticism, though different in terms of introversion-extraversion, certain modifications in terms of what is meant by these two factors are unavoidable. Eysenck (1959) has argued that, "all statistical and methodological analyses are 'artifacts', i.e. 'a product of human art and workmanship'; it is difficult to see how they could be anything else." Thus any failure by questionnaires to support a dysthymia-hysteria dichotomy might, with justification, be questioned on similar grounds. If, however, many investigators using both verbal and physiological methods reach conclusions which can be integrated into an alternative system to that proposed by Eysenck, then the possibility of human error being held responsible for a failure to demonstrate the validity of the dysthymic-hysteria dichotomy must be less.

On the basis of the available evidence the following suggested amendment to his theory appears worthy of consideration. He believes that both the dysthymic and the hysteric are characterized by high scores on tests purporting to measure neuroticism. Neuroticism he regards as "strong autonomic drive reactions" or "as a form of drive related to the *over*-excitability of the autonomic nervous system, particularly the sympathetic branch". Studies have been cited, however, which indicate that whilst dysthymics may be so characterized, the psychopath in particular proves the exception. Hysterics show the trend towards hyperreactivity to a lesser degree than dysthymics. The results lead one to suggest that neuroticism is not just related to over-excitation of the sympathetic but also to under-excitation. This of course changes the complexion of his theory, particularly since such differences can provide a plausible explanation for many of the differences in N and E between dysthymics and hysterics noted in current research reports and which are at variance with Eysenck's theory.

The first suggestion is that dysthymics differ from hysterics and psychopaths in terms of the degree of anxiety generated as a reaction to stress. Dysthymics are characterized by excessive anxiety responses, the hysterics by less anxiety, the psychopath least of all. *If "neuroticism" is to be retained it must cater not only for over- but also for under-excitation of the sympathetic nervous system.* The second suggestion is that conditionability might not be related to introversion as defined, for example, by the total M.P.I. E scale, *though introverts as assessed by the Guildford Rhythymia scale or the M.P.I. E scale are likely to show more rapid conditioning and extinguish these conditioned responses more slowly than extraverts so assessed by the above two scales,* providing these extraverts do not score at the upper end of the M.P.I. N scale. This statement needs some elaboration. If dysthymic neurotics are subject to *excessive* anxiety responses then some degree of social introversion is almost inevitable. Both the Rhythymia scale and the M.P.I. E scale appear in part to measure this factor. Thus anxiety (or one type of neuroticism) and social introversion appear to go together. As has been suggested earlier, Franks's work might be interpreted as evidence for instrumental conditioning in which anxiety acts as the drive. Thus the more anxious the individual the greater the speed of conditioning. If anxiety is minimal (the other type of neuroticism) then social introversion scores are likely to be less and total extraversion scores higher. These people would condition rather badly. Thus it is possible to achieve the same results as Eysenck but for other reasons. The essential differences between the two approaches are that the present suggestion recognizes differences in neuroticism (as defined above) between the two groups, that part of the differences in I-E between these same groups is related to this, and that according to the model presented earlier degree of arousability of the sympathetic nervous system will dictate speed of conditioning, though this might wrongly be ascribed, due to contamination of the available E scales, to introversion as defined by such as the total M.P.I. E scale.

Let one simple example suffice to illustrate the difference. Eysenck (1959) quotes Watson's famous experiment (1920) with little Albert, the young child who was fond of white rats. Watson created a fear of white rats in the boy by making a loud noise with a hammer whenever the child reached for the animal. This Eysenck quotes as an example of classical Pavlovian conditioning in which the animal was the conditioned stimulus, the loud noise the unconditioned stimulus and the unconditioned response was the fear. In other words the fear became associated with the rat and the child developed a phobia. Now few people would argue about the immensely important mediating role of anxiety

in learning theory, least of all Eysenck (1959). Indeed he has stressed this repeatedly. He would, however, argue that if young Albert was introverted he would condition much more quickly than young Tom who was extraverted. As Eysenck says (1959), "Watson was lucky in his choice of subject; others have banged away with hammers on metal bars in an attempt to condition infants, but not always with the same success". In other words Eysenck would consider the "young Alberts" of this world to condition much more quickly if they were introverted than extraverted. The alternative suggestion is that those with hyperreactive sympathetic nervous systems, show an exaggerated emotional response to the stress of a loud, unpleasant noise, that this stressor always followed attempts to reach for the animal and so there developed an understandable avoidance response, the speed and persistence of this conditioning bearing some relationship to the degree of anxiety. It would still be an instrumental rather than classical conditioning model and basically related to neuroticism though also probably related to introversion for reasons discussed earlier. Support for this viewpoint might be obtained from the work of Spence and Farber, 1953; Spence, Farber and Taylor, 1954; Spence and Taylor, 1951, 1953; Taylor, 1951.

If this modification is worthy of consideration then it should be capable of generating independent explanations or suggestions with regard to some of the major components of Eysenck's theory, for example, the central role played by reactive inhibition and its relationship to extraversion. According to the present argument those scoring high on extraversion scales are either behaviourally aggressive and so less anxious, though nevertheless capable of excessive anxiety responses, or show little evidence of emotional arousal to stressors. Stimulation of the sympathetic results, as is well known, in the post-ganglionic fibres liberating a substance almost identical with adrenaline, whilst glycogen stores in the liver are converted into glucose, etc. In other words the individual in such a state of arousal is physiologically more capable of dealing with an emergency; he has more immediate energy resources. Thus hyperreactive neurotic introverts and extraverts might be said to have these benefits more frequently than a person with a much less active sympathetic nervous system. If life can be regarded as being punctuated by a series of long-standing "stressful" situations demanding personal attention then the hyperreactive neurotic would appear physiologically particularly well endowed for this task. The energy resources at the command of such a person might be more than those possessed by the hyporeactive extravert. It is not difficult to appreciate how the latter in comparison may lag in terms of his application. Fatigue and indeed impatience would be more rapid in onset. In addition, of course, any pressure towards social conformity would also have less effect in such a person. Anxiety would be less and also the motivation towards conformity would be less. The hyperreactive introvert and the hyporeactive extravert might be said each to have the best and worst of two worlds. The former too much anxiety though greater energy supplies, the latter much less anxiety though less energy resources at his command. The hyporeactive extravert might well therefore be subject to excess reactive inhibition, because he has less sympathetically stimulated energy resources. Complicating the influence of reactive inhibition will always be the mediating role of anxiety. The less anxious hyporeactive extravert might show a rapid decrease in performance, perhaps wrongly attributable to reactive inhibition *in toto*, perhaps partly attributable correctly to the relative absence of anxiety not forcing conformity and persistence.

It might also be interesting to dwell for a moment on the relationship

between the action of adrenaline and the bodily metabolism. Wright (1947) has indicated that the ingestion of 1 mg. adrenaline in man increases heat production by as much as 20 per cent. for a short time. It is not difficult to see that the energy produced by the body might thus bear a relationship to the degree of sympathetic reactivity and that, in view of the previous suggestions, this might be linked directly to the degree of neuroticism as previously defined and only indirectly to 1-E. That is, varying degrees of reactive inhibition may correspond to varying degrees of sympathetic reactivity. At a more gross hypothetical level the well-known increase in application and persistence following the administration of sympathomimetic amines, e.g. amphetamines, might result from the stimulation of the sympathetic (they have a similarity in structure to adrenaline) just as the barbiturates might be expected to depress the sympathetic nervous system and so result in a lack of persistence and in sedation.

4. Relevance of the Conclusions from Previous Section to the Problem of Drug Addiction

One of the main conclusions emerging from the review is that there is a strong body of evidence which suggests an alternative explanation to that offered by Eysenck's theory with regard to the possible relationship between personality, psychiatric diagnosis and conditionability.

Eysenck would suggest that introverted individuals subjected to adverse environments would, according to a classical Pavlovian conditioning model, "take-over" the moral standards and behaviour patterns of this type of environment. In other words introverts associating with drug addicts would tend to become drug addicts. Psychopaths might, on the other hand, turn to addiction because of their under-socialization dependent on their extraversion. The alternative explanation is that introverts are more likely to be anxious and it is this emotional response which plays a central role in one type of addiction. In other words instrumental rather than classical conditioning appears to be important in drug addiction, that is, part of the phenomenon of addiction can be understood in terms of drive reduction theory. Other aspects of addiction might be accounted for in terms of a combination of a hyporeactive sympathetic nervous system (the individual would show little concern about what society thought of his actions), plus some element of drive reduction other than that related to anxiety. These views will be elaborated in the next section.

THE RELEVANCE OF PHYSIOLOGICAL PROPERTIES OF DRUGS TO ADDICTION

Although serious doubts have been expressed concerning the validity of interpretations drawn from results of Pavlovian-style experiments, these doubts are by no means limited to the present review. It is one of the issues on which learning theorists tend to divide. Ever since the old law of association (ideas experienced together tend to become associated) and the later principle of association by contiguity were formed, doubts have been expressed by theorists about the exclusion of the role of reinforcement, reward or punishment, etc. from these systems. One of the main advocates of a stimulus-response association psychology was Guthrie (1930, 1942). The motivational state of the individual had no formal place in his theory. Of six experiments quoted by Hilgard (1956) relevant to this theory, four however presented evidence contrary to it (Seward, 1942; Seward, Dill and Holland, 1944; Zeaman and Radner, 1953; Wickens and Platt, 1954). Mueller and Schoenfeld (1954) similarly

concluded, "While the principles of conditioning which he expands (Guthrie) seem to have a parsimony that would be desirable in a theoretical formulation of behaviour, a closer analysis reveals that a formidable set of additional assumptions and constructs are required if his theory is to possess any real applicability to experimental data." Finally in support Hilgard (1956) has this to say, "Actual experiments in which autonomic conditioning takes place (salivation, galvanic response) are full of indirect accompaniments of Type R. When the circumstances seem almost ideal for demonstrating Type S conditioning, as in attempts to condition pupillary constriction by presenting a tone along with a light, it is extremely difficult to obtain any conditioning at all (Wedell, Taylor, Skolnick, 1940; Hilgard, Dutton and Helmick, 1949; Young, 1954) . . . pure cases of Type S conditioning are hard to find. The heart-rate conditioning of Notterman, Schoenfeld and Bersh (1952) includes the possibility of operant intermediaries." Indeed Hull published a formal derivation of Pavlovian conditioning on the basis of the reinforcement principle as early as 1937.

Because of these doubts the first essential is to examine the physiological properties of certain known addictive drugs to see whether these properties possess drive-reducing qualities which an alternative reinforcement theory of drug addiction would require. Table I presents the "benefits" and withdrawal symptoms associated with some of the well-known addictive drugs.

TABLE I

The Benefits and Withdrawal Symptoms Associated with Certain Addictive-Drugs

Drug	"Benefits"	Withdrawal Symptoms
Morphine and its derivatives	Feeling of exhilaration and euphoria, diminution of individual's self-critical faculties; feeling of supreme contentment and self-satisfaction under the most deplorable conditions.	Depression; anxiety with restlessness; profound malaise; shivering and twitching; variable pain and muscular cramps; nausea; vomiting and diarrhoea.
Cocaine	Exhilaration; elation or euphoria, increased flow of ideas.	Insomnia, palpitations; general malaise, gastric disturbance; slight confusion.
Pethidine	Analgesic.	Sweating; malaise; anxiety; depression; cramp-like pains. Associated with larger dosages are more serious symptoms—convulsions, choreoathetotic movements.
Barbiturates	Alleviation of anxiety and tension. Disinhibition.	Anxiety; tremors; palpitations; postural dizziness, vomiting.
Amphetamines	Increased energy, mental alertness and agility.	—
Marijuana	Sense of euphoria, volubility and hyperreactivity followed by a sense of calm and relaxation.	—

In view of the frequency of withdrawal symptoms noted in this table, can physiological dependence account for drug addiction? It certainly appears that the body adapts to the effects of some of these drugs, though not in a uniform way, so that many more times the original dosage is required to produce the same effect. If the drug is suddenly withdrawn, once tolerance has been developed, unpleasant withdrawal symptoms result. To avoid these

unpleasant withdrawal symptoms the addict need only take the particular drug again. In other words he must take the drug habitually to prevent the onset of this physiological distress. Nevertheless there appears to be a more basic reason to explain drug addiction for withdrawal symptoms tend not to be unbearable whilst the self-limiting nature of the condition results in their disappearance in a matter of ten days. Similarly if drug addiction were caused by physiological dependence it could not explain the fact that some 75 per cent. of drug addicts discharged from hospital free from physical dependence started using the drug almost immediately after discharge (Ausubel, 1952). It would also appear illogical as Ausubel argues, that most people would be "willing to pay the fantastic price of the drug and risk imprisonment, social disgrace, and ostracism merely to avoid a moderately severe ten-day illness. Secondly, every year thousands of persons with serious fractures, burns, and surgical conditions receive opiates long enough to develop physiological dependence, but are nevertheless able to break this dependence quite easily. Thirdly, the dosage of morphine required to prevent withdrawal symptoms is never more than one or two grains daily. Hence, why will drug addicts take up to twenty grains a day if they take the drug, as they claim, 'just to feel normal'? Fourthly, withdrawal symptoms can be adequately relieved if morphine is taken by mouth. Therefore, why will addicts give themselves pain and run the risk of infection by injecting the drug 'main-line', or directly into their veins, with crude, home-made syringes? The answer to both these questions is that the large dose and the 'main-line' route increase the 'kick' or euphoric effect of the drug. Fifthly, a new opiate has been developed which has all the analgesic and euphoric properties of morphine, but for which withdrawal symptoms are minimal. Nevertheless, the evidence is conclusive that addiction develops just as rapidly for this drug as for other opiates."

If physiological dependence is not *basic* to the development of addiction, what other qualities do addictive-drugs possess which make them a necessity to the addict? A principal pharmacological property of morphine and its derivatives is euphoria—the addict can feel "supremely contented and self-satisfied under the most deplorable conditions". This effect can also be produced by cocaine, and marijuana addiction. The amphetamines produce a similar reaction, though of less intensity—it takes the form of increased energy, mental alertness and agility. The barbiturates and alcohol might also be said to produce similar effects to each other—an alleviation of anxiety and tension and disinhibition. In other words the beneficial adjustive qualities of these drugs might initially be of more importance than the subsequent physiological dependence. Within this context it is therefore important that, in the section of the review dealing with the experimental studies of addiction, it became apparent that the addict was, in the majority of studies, considered to be psychologically abnormal and this abnormality to precede his addiction. Studies were cited subsequently which suggested that neurotic abnormality varied between extreme and minimal degrees of anxiety, neurotic categories bearing a relationship to this dimension. Thus those neurotics prone to anxiety, tension and social difficulties might prove particularly susceptible to the beneficial effects of the barbiturates and alcohol. Their over-socialization might also prevent them from resorting to the socially unacceptable drugs such as marijuana, heroin and opium if the opportunity arose, or indeed to prevent them from being part of a set of circumstances likely to provide the temptation in the first place. Psychopaths, on the other hand, might alternatively resort to these latter drugs with less of a conscience and because of their under-socialized

behaviour may have more opportunity to resort to these drugs. If the thesis of the present paper is correct then the true psychopath, with less anxiety, should have less need to become addicted to the barbiturates and alcohol, though one can see more clearly the benefits of the euphoric drugs to him.

Such a clear demarcation between the types of drugs taken by these two main classes of patients is probably far too simple. Anxious patients do presumably become opium and marijuana addicts. The euphoric effect of these drugs can readily be seen to possess drive-reducing qualities. The conclusion appears to be that all of the quoted drugs possess qualities which are likely to be more beneficial to the psychologically abnormal subject than to the normal person and so drug addiction may be a learned phenomenon developing as a simple function of the consequence of the drug in question. If these rewards are influential in determining learning, is the extent of the learning (the addiction) a function of the amount of reward? In other words is there a relationship between the strength of the addiction and degree of neuroticism? Thorndike (1933), it will be remembered, held the view that reward operated in an all-or-none fashion. Variations in the amount of reward, according to this view, had little effect on the learning process providing the reward was sufficient to produce the reinforced response. Hull (1950) tends to agree with this formulation for habit is said to be a function of the frequency of reinforcements rather than the amount of reinforcement. The work of Grindley (1929), Gantt (1938), Crespi (1942) and Zeaman (1949) on the other hand suggests that performance does increase as the amount of reward increases. In order to reconcile these findings McGeoch and Irion (1952) suggest that habit has to be separated from performance and that the amount of reinforcement determines the latter rather than the former. Hull has done precisely this. Performance he regarded as a multiplicative function of habit and reward. The facts, unfortunately, do not suggest any clear picture. Human learning experiments tend to favour the idea that reinforcement acts in an all-or-none fashion. Learning does not always increase with an increase in reward and what is equally important, when this increase does occur it is not always proportional to the amount of reward (Thorndike and Forlano, 1933; Rock, 1935; Eisenson, 1935). Thus one cannot say with any confidence that the severity of the addiction is a simple function of the severity of the neurosis, though some degree of neuroticism appears necessary to guarantee that the rewards are sufficient to produce the reinforced addictive response.

Reinforcement theorists are less divided about learning being an increasing function of the number of reinforced trials. This assumption is basic to the work of Thorndike and Hull. The facts of conditioning and instrumental learning experiments tend to bear out this view. Similarly there is much evidence supporting the idea that responses which occur in close temporal contiguity to a reinforcing agent tend to become more strongly learned than those separated from the reinforcement in time. In other words the more frequently an unstable addict resorts to the drug the greater the learning, whilst drug effects also tend to occur in "close temporal contiguity" to the drug stimulus and so lead to further reinforcement.

In conclusion, if physiological dependence is not basic to the initial development of addiction, what might be its role in the development of the phenomenon? Its probable role might best be illustrated within an instrumental learning model proposed to explain drug addiction. The subject takes a drug which is found to possess drive-reducing qualities.

The strength of the habit then develops as a multiplicative function of

drive reduction, the frequency with which the patient resorts to the drug and the temporal contiguity of the stimulus and reward. Hand in hand with the development of this habit the body builds up a tolerance for certain of these drugs which necessitate larger dosages to produce the same effect, an effect which has become an "additional" necessity as it has itself become reinforced in the development of the addiction. Correlated with the increased tolerance and dosages are the withdrawal symptoms. It is suggested that these may have a differential effect on the hyperreactor and on the hyporeactor. In view of the apparent lower tolerance of stress in the former group, avoidance of the withdrawal symptoms may become more of a necessity, such avoidance acting as the reward and so directly assisting in the further development of the habit. Thus the avoidance of the unpleasant withdrawal symptoms would not be essential to the development of addiction, as well illustrated by Ausubel, but the presence of these symptoms might well reinforce a further dependence on a drug both through an inability to tolerate the stresses associated with them and the immediacy of the reward associated with their termination. The patient need only take the drug again to avoid these unpleasant symptoms.

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CONCEPTUAL STRUCTURE IN THOUGHT-DISORDERED SCHIZOPHRENICS*

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INTRODUCTION

"THOUGHT-DISORDER" in schizophrenia was initially a psychiatric concept derived from clinical observation. As crystallized in standard psychiatric authorities, say Mayer-Gross, Slater and Roth (1954) the primary features of the talk (and inferentially the thinking) of thought-disordered schizophrenic patients are:

- (i) Inconsequential following of side issues.
- (ii) Tendencies for the thought to be directed by alliterations, analogies, clang associations, associations with accidents of the speaker's environment, symbolic meanings, and the condensation of several (perhaps mutually contradictory) ideas into one.
- (iii) Words used out of context, e.g. concrete meanings taken where abstract meanings would be appropriate.
- (iv) Clinging to unimportant detail.
- (v) The use of laconic answers, e.g. I don't know, maybe, perhaps—indicative of emptiness and vagueness of ideas.
- (vi) Thought is generally marked by gaps, poverty, indefiniteness and vagueness.
- (vii) Indications of thought-blocking.
- (viii) Indications of pressure of thoughts.

It should be noted that these represent abnormalities of form rather than content and thus are theoretically distinct from simply delusional talk. Moreover, "schizophrenia" itself appears to be a *disjunctive* concept and the diagnosis may, in practice, be applied to patients manifesting one or some but not necessarily all of the five major symptoms, as defined by say, Curran and Partridge (1955) these being thought-disorder, inadequacy or inappropriateness of affect, low volition, disturbances of motility and primary delusions. Thus in psychiatric practice "thought-disordered schizophrenics" seem to be regarded as a sub-group of the class of schizophrenics.

Four broad approaches have been made towards operationally defining the psychiatric concept of thought-disorder and subjecting it to experimental attack.

(i) "Dissociation"

This concept was primarily used by Kretschmer (1936) postulating that schizophrenic thinking is essentially marked by dissociation (*Spaltungsfähigkeit*)

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a tendency for mental activity to occur in isolation with a consequent fragmenting and lack of logical relationship between systems of ideas. The origin of this tendency was given in typological terms, i.e. two constitutional personality types (linked to the somatotypes leptomorphic and pyknic) were postulated, namely schizothymic (extreme manifestation schizophrenia) and cyclothymic (extreme manifestation manic-depressive psychosis). Experimental work generated by this thesis has been mainly of the dual task type; thus the subject might be given the task of memorizing the positions of coloured letters drawn on a card and at the end of the task be asked additionally to recall the colours in which the letters were drawn (a task not mentioned in the initial instructions). The appropriate prediction would be that schizophrenics would perform the dual task more competently (at least relative to the single task) than manic depressives (extreme "associaters") or normals since schizophrenics are, by nature, inclined to function dissociatively. This field of experimentation has been well reviewed by Payne (1954) who found that in a large number of tests of dissociation given to normals no factor of dissociative ability emerged. Bellak and Parcell (1946) investigated the pre-psychotic personalities of schizophrenics and could find no evidence indicating that the typological characteristics which Kretschmer postulated were a concomitant of schizophrenia. Moreover, the type of experimental design generally used seems to imply that since schizophrenics are inferior to normals in utilizing the logical relationships between systems of ideas they will be superior to normals in simultaneously utilizing systems of ideas which are not logically related. This seems a somewhat doubtful inference. Disorganized men do not necessarily flourish in a disorganized world.

(ii) "*Deterioration in Mental Efficiency*"

Babcock (1933) initiated an approach to the problem of schizophrenic thinking by categorizing it as a process of progressive mental deterioration particularly marked by slowness and inability to undertake new learning, due to organic causes analogous to those operating in senile and paretic conditions. This explanation was realized experimentally in the form of first measuring the level of "abstract intelligence" operationally defined as the subject's level on the Terman Vocabulary Test and assumed to represent old pre-illness learning; then measuring "mental efficiency" this being operationally defined as the subject's level on a series of mental efficiency tests, such as counting from 20 to 1, digit span, etc., this type of performance being taken to represent new learning and present level of function and to be markedly affected by deterioration of a schizophrenic type. The discrepancy between the two levels (termed the Efficiency Index) being the measure of deterioration. This approach can be adversely criticized for its unquestioned assumption that vocabulary level is a fair measure of pre-illness capacity—Yates (1956) has reviewed the difficulties implicit in this assumption and, more pertinently, the notion's validity as a *specific* explanation of the schizophrenic process is questioned by the work of Shapiro and Nelson (1955) and Campbell (1957) which indicates that loss of mental efficiency as defined by Babcock is a complex and very general phenomenon in mental illness manifesting itself in depressives, organics and even to some extent in neurotics as well as in schizophrenics.

(iii) "*Concretism*"

Implicit in the work of Vigotsky (1934) Bolles and Goldstein (1938) and others which form the focus of the Kasanin (1946) symposium, is the idea that

schizophrenic thinking is essentially concretistic and marked by inability to form abstractions. Operationally "abstraction" is usually defined in terms of a subject's ability to group and categorize objects in object-sorting tests (e.g. grouping blocks by form, colour, size, weight, etc.) or ability to give the meanings of proverbs in terms of acceptable generalizations. Examples of work critical of this approach are Rapaport, Gill and Shafer (1945) who found the tendency to be for schizophrenics to produce unusual generalizations rather than to fail to abstract and Hunt and Jones (1958) who showed that when trained clinicians used the dimensions "schizophrenia", "intelligence", "communicability" and "concrete-abstract" to scale schizophrenic vocabulary responses "concrete-abstract" scaling had the lowest interjudge correlation and correlated insignificantly and *negatively* with the scale "schizophrenia". Experimental work on "concretism" is reviewed in relation to comparative experiments utilizing "over-inclusion" theory by Payne, Matussek and George (1959).

(iv) "*Over-inclusion*"

The most recent attack on the problem derives, in part, from the suggestion by Cameron (1938) that schizophrenics are unable to preserve the conceptual boundaries of a task and thus include in the data before them such a variety of categories that specific problems become too extensive and too complex for a solution to be reached. This suggestion has been steadily developed by workers such as Lovibond (1954) until it has now been very explicitly formulated by Payne, Matussek and George (1959) in the following terms:

"Concept formation can be regarded as largely the result of discrimination learning. When a child first hears a word in a certain context, the word is associated with the entire situation (stimulus compound). As the word is heard again and again, only certain aspects of the stimulus compound are reinforced. Gradually the extraneous elements cease to evoke the response (the word) having become "inhibited" through lack of "reinforcement". This inhibition is in some sense an active process, as it suppresses a response which was formerly evoked by the stimulus. "Over-inclusive thinking" may be the result of a disorder of the process whereby "inhibition" is built up to "circumscribe" and "define" the learned response (the word or "concept"). In short it could be an extreme degree of "stimulus generalization".

Exemplary experimental work can be found in Zaslow (1950), Moran (1953) and Epstein (1953).

Without attempting in detail to evaluate the experimental work arising from these four approaches, it can be argued that all of them are limited in that they describe the schizophrenic *condition* rather than define the schizophrenic *process*. Ultimately each rests upon some kind of constitutional or typological or undefined organic assumption so that the question of causal factors is by-passed. By-passed, that is, if we accept the view that such assumptions are fundamentally tautological. Moreover, these explanations do not refer back to the clinically observed behaviour upon which the concept of schizophrenic thought-disorder was originally based.

PERSONAL CONSTRUCT THEORY

In an attempt to utilize a theoretical orientation which would not only operationally define the nature of schizophrenic thinking but would generate hypotheses as to the causal factors involved and which would comment

specifically on the broad behavioural manifestations of schizophrenic thought-disorder, the work to be described was carried out within the framework of Personal Construct theory as proposed by Kelly (1955).

The theory is based firmly on the assumption that all men may be thought of as "scientists" in the sense that each is concerned with the prediction and control of his environment. Further each individual seems to develop his own personal repertoire of constructs by means of which he structures (conceptualizes) his world and tries to anticipate events. These constructs may be thought of as the elements of a system by which the individual codifies his experience. Thus the psychology of personal constructs is concerned with the ways in which personal construct repertoires can be described in generalized terms and to account for the ways in which they develop and change and the ways in which they can be utilized in accounting for individual behaviour.

The theory involves postulating a personal construct system for each individual, a complex series of related "goggles" through which an individual views reality. The notion of process hinges on the idea that construing is a biologically purposeful process whereby an individual seeks to anticipate events. A construct is not merely a label, it is in essence a prediction. To construe a business as profitable or a woman as affectionate is to predict future events in relation to the elements construed and predictions are inevitably validated or invalidated or events prove the prediction to have been irrelevant, i.e. the events turn out to be outside the range of convenience of the constructs used. It is in the individual's reaction to the emerging validation situation that the theory expects the process of change to subsist.

The three elements of the term "personal construct system" stress firstly that individual differences (in terms of varying validation experience) must be postulated as an integral part of the theory and their parameters described. Secondly, that a construct (as distinct from the older term concept) is a predictive instrument and thirdly that constructs are hierarchically related and systematized.

Kelly formally presented his theory as a fundamental postulate and eleven elaborative corollaries. Space does not permit a detailed account or discussion of the theory here but it should be understood that the terms of reference of the experimental work to be described are derived from this theoretical framework.

Repertory Grid Testing

Kelly defined a "construct" as "a way in which two things are alike and by the same token different from a third". In order to elicit and examine verbal constructs he and his associates developed the technique of repertory grid testing. The assumption underlying all forms of repertory grid testing is that conceptual relationships can be usefully inferred from statistical associations in usage. Thus, isolating a single extreme example, if a subject nominates 40 people known personally to him and categorizes each in turn as MORAL (emergent pole) or NOT MORAL (implicit pole) and HONEST or NOT HONEST and we find that the 20 designated as HONEST are also designated as MORAL and the 20 designated as NOT HONEST are designated as NOT MORAL, then we can infer a high positive relationship (which can be measured in terms of its binomial probability) between the concepts HONEST and MORAL.

A variety of forms of the repertory grid test have been devised and used, e.g. Landfield (1955) and Levy (1956) but the particular elaboration of the basic technique used in the work to be described was designed for this experiment and so far as is known no comparable data are available from other studies.

EXPERIMENT

The following is a summary of work fully described in Bannister (1959).

Experimental Population

Normals: 20 adult normals (adult=age 17+), subjects never having been hospitalized for mental illness, treated for mental illness or officially diagnosed as mentally ill.

Thought-disordered schizophrenics: 8 adults, at time of testing patients in a mental hospital, firmly diagnosed as schizophrenic and adjudged to be thought-disordered by the psychiatric consultants responsible for them.

Non-thought-disordered schizophrenics: 12 adults, at time of testing patients in a mental hospital, firmly diagnosed as schizophrenic but not adjudged to be manifesting signs of thought-disorder by the psychiatric consultants responsible for them.

Neurotics: 10 adults, at time of testing patients in a mental hospital, firmly diagnosed as suffering from one of the psychoneuroses (e.g. anxiety states, hysterias and so on) by the psychiatric consultants responsible for them.

Depressives: 10 adults, at time of testing patients in a mental hospital, firmly diagnosed to be suffering from either a reactive or an endogenous depression by the psychiatric consultants responsible for them.

Note: The term "schizophrenics" in the ensuing report refers always to non-thought-disordered schizophrenics.

Extraneous Variables

Four extraneous variables might reasonably be thought to have an effect upon performance in tests involving verbal judgments namely, age, sex, intelligence and social status. These were dealt with as follows:

Age: There were no significant differences between the means or variances of any of the five groups.

Sex: Two of the psychiatric groups had unequal sex distribution and all test scores were examined by sex groupings. There were no significant differences and sex as a variable seemed to have no appreciable effect.

Intelligence: The measure of intelligence used was the Mill Hill Vocabulary Scale Form 2, Section A (pro-rated). There were no significant differences in either means or variances between any of the groups.

Social Status: This was defined in terms of the occupation and education of the subject and the occupation of the subject's immediate family according to the scale suggested by Belson (1955). There were some significant social status differences between certain groups but these did not correspond with significant differences on any test measures shown in the final results.

It seems clear that none of the extraneous variables which have been taken into account can fairly be said to account for differences in test performance found between groups.

Test Administration

1. The subject was asked to write down on 36 cards the names of 36 adult (age 17+) people known personally to him. It was explained that they might be people of any kind, liked or disliked, present or past acquaintances, but they must have been personally known to the subject.

TABLE I—*continue*

																		Grid B People			
19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36				
O	X	X	O	O	O	X	O	X	O	X	X	O	O	X	O	X	X	1			C
X	X	X	X	O	O	O	O	X	O	O	X	X	O	O	O	X	X	2			N
X	O	X	X	X	O	O	X	O	X	X	O	O	X	O	X	O	O	3			S
																		to			R
																		10			U
																					C
																					T
																					S

Matching Score, Grid A

Each line in Grid A (people 1 to 18) is compared with every other line and a matching score noted—two ticks coinciding (vertically) represent a match, two blanks coinciding represent a match, tick and blank or blank and tick is no match; thus in Table I

For lines 1-2 Grid A matching score is 8

For lines 1-3 Grid A matching score is 4

For lines 2-3 Grid A matching score is 10

Matching Score, Grid B

Each line in Grid B (people 19 to 36) is compared with every other line and a matching score noted—matching criteria as for Grid A. Thus in Table I

For lines 1-2 Grid B matching score is 12

For lines 1-3 Grid B matching score is 4

For lines 2-3 Grid B matching score is 6

Total Matching Score

The matching score for each pair of lines in Grid A is added to the matching score of the equivalent pair of lines on Grid B, and the deviation (plus or minus) from a chance expectancy of 18 is noted. Thus, in Table I

The total matching score for lines 1-2 is +2 (8+12=20; 20-18= +2)

The total matching score for lines 1-3 is -10 (4+ 4= 8; 8-18=-10)

The total matching score for lines 2-3 is -2 (10+ 6=16; 16-18= -2)

Split Matching Score

The deviation of the matching score of each pair of lines on Grid A from chance expectancy on Grid A (that is 9) is added to the deviation of the matching score of the equivalent pair of lines on Grid B (that is 9) *regardless of sign*, and this addition represents the split matching score. Thus in Table I

Lines 1-2 split matching score is 4 (8-9=-1 12-9=3; 1+3= 4)

Lines 1-3 split matching score is 10 (4-9=-5 4-9=-5; 5+5=10)

Lines 2-3 split matching score is 4 (10-9= 1 6-9=-3; 1+3= 4)

The difference between the two measures lies in the fact that a total matching score treats the two grids as a unit, and thus if the direction of the relationship is reversed (plus to minus) the relationship will tend to cancel itself out, while a split matching score treats the two grids as separate units and makes

relationships in either direction (positive or negative) additive regardless of sign.

Thus, for each subject, initial raw data covering comparisons of the 45 possible pairs of lines (from 10 lines) is extracted, and laid out as exemplified in Table II.

TABLE II
Sample Part of Raw Data Table Derived from Recorded Grids

		Matching Score Grid A		Matching Score Grid B		Total Matching Score	Split Matching Score
Lines	1-2	..	8		12	+2	4
	1-3	..	4		4	-10	10
	to 1-10						
	2-3	..	10		6	-2	4
	to 9-10						

Rationale of Matching Scores

The rationale of the type of matching score described is relatively simple. If a subject describes one person as being both SINCERE and GOOD we cannot, from this one sample of the subject's behaviour, infer anything about the relationship between the terms SINCERE and GOOD for him. However, if in describing a large number of people there appears a persistent tendency for him to describe SINCERE people as GOOD then the binomial probability of this occurring by chance becomes increasingly remote and we are increasingly justified in inferring that for the subject there is some kind of conceptual relationship between the terms SINCERE and GOOD. Thus a matching score derived from a number of yes-no categorizations in the manner described, is a form of correlation coefficient (or more nearly chi square) measuring the tendency for the terms to be associated or to occur independently or for one to occur repeatedly in the absence of the other (negative association or correlation). From this tendency to association we infer structure and it is precisely the nature of this structure which Personal Construct theory attempts to define and describe.

In this experiment each subject is supplied with the same 10 constructs and he sorts the 36 people known personally to him in terms of the 10 bipolar scales suggested to him by the construct labels supplied. The use of matching techniques enables us to compare each pair of constructs in turn and to assign to the comparison a numerical value which ranges from no matchings (taken to indicate that the two labels are exact opposites) through matchings around chance level (taken to indicate that there is no manifest relationship between the construct poles labelled) on to complete matching (taken to indicate exact equivalence for the subject of the two construct pole labels).

FOUR DERIVED MEASURES

CONSISTENCY OF RELATIONSHIP

(a) *Scoring*

Reference to Table II shows that for each of the 45 pairs of constructs two matching scores are available, one from Grid A and one from Grid B. For each subject a Pearson Product Moment correlation coefficient is run between the pairs of readings (matching scores) for the 45 pairs of constructs. The square of this correlation coefficient multiplied by 100 is the Consistency of Relationship score.

(b) *Rationale*

If matching scores derived in the manner described reflect structure, and if as personal construct theory suggests, a relatively *stable* structure is characteristic of construing systems, then we would expect a significant positive correlation between matching scores (structural pattern) on Grid A and equivalent matching scores (structural pattern) on Grid B, allowing that is, for the attenuating effect of using smaller numbers of "objects" (people) as the sample to be construed in each of the grids. We would consequently expect failure to achieve such a significant positive correlation in test performance to be associated with pathological processes. It should be noted that the term "allowing for the attenuating effect" means allowing in argument; no actual correction for attenuation has been used in the statistical computation of results since the attenuating effect is equal for all subjects; it will affect the absolute but not the relative values of the scores.

In fact, as will be seen when results are reported, of the 60 subjects used in the main experiment, the consistency of relationship correlation coefficients of 47 were significant at beyond the 1 per cent. level 2 tail; those of 3 were significant beyond the 5 per cent. level 2 tail; those of 8 were positive but not significant; those of 2 were negative but not significant (both the latter were thought-disordered schizophrenics).

Since correlation coefficients are not linearly related they are unsuitable for direct use as scores. Therefore, they have been squared and multiplied by 100 to give "variance in common" scores which are linearly related.

It should be noted that the coefficient of correlation derived here is not the equivalent, say in intelligence testing, of a test-retest reliability coefficient since virtually no time elapsed between the making of the judgments recorded in Grid A and the making of the judgments recorded in Grid B. Nor does it resemble the split-half reliability coefficient since matching scores on Grid A reflect comparisons made by the subject of the people on Grid A and matching scores on Grid B, separately and independently reflect comparisons made by the subject of the different people included in Grid B. There is no equivalent here of the extraction say, of odd and even numbered questions from a unitary test, such as is commonly carried out in split-half reliability tests. If the correlation used here has any kinship with correlations used in standardizing intelligence tests, it is with the "equivalent form" type of correlation, where two forms of the intelligence test, equated as far as possible for difficulty level are given to the same subject often with the clinical aim of detecting pathological process.

The measure of Consistency of Relationship assesses something which might, by many psychologists, be termed stability or even rigidity in conceptualization.

INTENSITY OF RELATIONSHIP

(a) *Scoring*

A subject's intensity of relationship score consists simply of the total of his split matching scores, the derivation of which has already been given with reference to Tables I and II.

(b) *Rationale*

The rationale of the intensity of relationship score is essentially the same as the rationale of matching scores themselves; the deviation of matching scores

from chance level is taken to indicate relationships between constructs, by inference conceptual structure; the degree of this deviation is taken as an index of the strength of relationships and, by inference, strength of conceptual structure.

COEFFICIENT OF VARIATION

(a) *Scoring*

For each of the ten constructs in a subject's protocol, a construct matching score is computed. This is simply the total of the construct's total matching scores (see Tables I and II and related text) with the *other* 9 constructs, these being added together regardless of sign. The standard deviation of these 10 construct matching scores is then calculated (using small sample standard deviation formula) and using Karl Pearson's formula, a coefficient of variation is derived, as follows:

$$\frac{100 \times \text{S.D.}}{\bar{X}} = \text{per cent.} = \text{Coefficient of Variation}$$

Karl Pearson's Coefficient of Variation formula

This coefficient of variation (which is in the form of a percentage) is what is meant by a subject's Coefficient of Variation score.

(b) *Rationale*

The question of why an individual's construct relationships should weaken is to be speculatively discussed later but it is assumed that when such a weakening process takes place its effect is not necessarily equally distributed between all constructs. Since constructs themselves are often constellated into hierarchies and sub-systems, some construct relationships may weaken more rapidly than others and some constructs within a personal construct system may thus lie within a very weak network of relationships, while others occupy a position in what is still a relatively strong network of relationships. From this it is argued that subjects who are undergoing a general process of weakening in terms of construct system structure will show, within any sample of constructs, a tendency to greater variability in strength of construct relationships. The Coefficient of Variation score is designed to measure precisely this variability.

It was decided not to use a simple measure of variance (such as the standard deviation) since it was found that (as is often the case) the lower a subject's absolute scores were, the lower his variance tended to be. For schizophrenic subjects in the main experiment, the correlation between the standard deviation of subject's construct scores and Intensity of Relationship scores was $+.462$. The use of the coefficient of variation formula enables us to partial out the effect of the absolute size of raw scores and to measure the relative variability of subjects' matching scores independently of the absolute size of the matching scores themselves.

SOCIAL DEVIATION

(a) *Scoring*

The mean of the total matching scores of the 20 normal subjects for each pair of constructs is a criterion for this measure. The actual means, to the nearest whole number, are shown in Table III. The Social Deviation score is simply the

TABLE III

Mean of 20 Normals (Total Matching Scores) for 10 Constructs. Main Experiment

	Like- able	Seri- ous	Preju- diced	Good	Aggres- sive	Lazy	Sin- cere	Unedu- cated	Reli- gious	Unre- liable
1. Likeable ..		+2	-7	+10	-6	-3	+7	-4	+3	-6
2. Serious ..			-1	+3	-1	-4	+4	-4	+3	-4
3. Prejudiced ..				-6	+7	+4	-5	+3	-2	+5
4. Good ..					-8	-4	+11	-4	+5	-8
5. Aggressive ..						+3	-6	+2	-3	+6
6. Lazy ..							-5	+4	-2	+6
7. Sincere ..								-5	+5	-8
8. Uneducated ..									-2	+5
9. Religious ..										-4
10. Unreliable										

total of the discrepancies between the subject's total matching score on each pair of constructs and the mean matching score of the same pair of constructs as derived from the 20 normal subjects and shown in Table III. The higher the total of the discrepancies the greater is (assumed to be) the deviation from social usage.

(b) *Rationale*

If we assume that the mean of the 20 normals broadly represents the *public* relationship between each pair of constructs, then the discrepancy between a particular individual's scores and this representative mean is a measure of the degree to which the subject is idiosyncratic in his usage relationship for a particular pair of constructs. If we assume that the 10 constructs measured are a fair sample of constructs used in the sub-system of constructs about people, then the total discrepancy will fairly reflect the tendency of the individual to be like or unlike the majority of his fellows in his construct relationships.

Admittedly, in computing this score for a normal subject, then we are noting a discrepancy between an individual score and a mean score to which that individual has contributed, whilst when we are computing the discrepancy for an individual psychiatric subject, we are noting the discrepancy between an individual score and a mean score to which the individual has not contributed. However, since the means are the means of 20 subjects, it is not thought that the final results will be in any significant degree biased by this factor.

HYPOTHESES AND RESULTS

Working within the framework of a novel theory and technique and attempting to discriminate between groups very broadly differentiated on a diagnostic basis, hypotheses are necessarily general and partake of the character described in gunnery circles as "bracketing the target". Two broad considerations affected the hypotheses, firstly it was decided to predict identical positions on the various continua for both schizophrenic groups, since there was prior to testing no evidence that their diagnostic separation in any way corresponds with the types of operational distinction being made; to treat neurotics and depressives in terms of prediction as a single group since although they differ from schizophrenics in broad behavioural terms, they equally differ from normals in being "abnormal": to treat the normal controls as a third group for predictive purposes. Secondly, although Kelly proposed personal construct theory as an elaborate description of *normal* behaviour he did make specific comments in the light of his theory about various psychological abnormalities and with reference to schizophrenia he suggested that it was

It should be noted that only two groups differed significantly in score distributions (F ratio). Thought-disordered schizophrenics were significantly (5 per cent. level) more homogeneous in scores than non-thought-disordered schizophrenics whose scores were widely scattered.

INTENSITY OF RELATIONSHIP

The hypotheses here were identical with those made for the Consistency of Relationship measure.

TABLE V
Intensity of Relationship—Group Means and Standard Deviations

Group	Normals	Thought-Disordered Schizophrenics	Non-Thought-Disordered Schizophrenics	Neurotics	Depressives
Mean	281.65	209.62	258.66	284.7	242.2
S.D.	78.917	27.308	54.792	57.74	49.234

Levels of "t" (Uncorrelated Means)

Groups	Thought-Disordered v. Non-Thought-Disordered Schizophrenics	Non-Thought-Disordered Schizophrenics v. Normals	Thought-Disordered Schizophrenics v. Normals	Thought-Disordered Schizophrenics v. Neurotics	Non-Thought-Disordered Schizophrenics v. Neurotics
"t"	5% level t=2.331	N.S.	1% level 1 tail t=2.498	1% level t=3.374	N.S.
"t"	Normals v. Neurotics N.S.	Thought-Disordered Schizophrenics v. Depressives N.S.	Non-Thought-Disordered Schizophrenics v. Depressives N.S.	Normals v. Depressives N.S.	Neurotics v. Depressives N.S.

A summary of hypotheses and results is shown below

Hypothesis:

All Schizophrenics

Normals

Neurotics/Depressives

Result:

	Depressives	
Thought-Disordered Schizophrenics	Schizophrenics/Normals/Neurotics	
Low	← Intensity →	High

Here again thought-disordered schizophrenics had relatively homogeneous scores differing in this respect significantly from normals (5 per cent. level).

COEFFICIENT OF VARIATION MEASURE

The hypothesis here was that all schizophrenics would show high variability in construct relationship strength, normals medium range variability and neurotics and depressives low variability with significant differences between the three clustered groups. The argument being that the progressive weakening

Groups			Thought-Disordered v. Non-Thought-Disordered Schizophrenics	Non-Thought-Disordered Schizophrenics v. Normals	Thought-Disordered Schizophrenics v. Normals	Thought-Disordered Schizophrenics v. Neurotics	Non-Thought-Disordered Schizophrenics v. Neurotics
"t"	..	..	N.S.	5% level 1 tail $t=2.014$	N.S.	N.S.	N.S.
			Normals v. Neurotics	Thought-Disordered Schizophrenics v. Depressives	Non-Thought-Disordered Schizophrenics v. Depressives	Normals v. Depressives	Neurotics v. Depressives
"t"	..	..	N.S.	N.S.	N.S.	N.S.	N.S.

A summary of hypotheses and results in print form is shown below

Hypothesis:

Normals

Neurotics/Depressives/All Schizophrenics

Result:

Neurotics/Thought-Disordered Schizophrenics/Depressives

Normals

Schizophrenics

Low

← Social Deviation → High

ASSESSMENT OF RESULTS

The broad picture which has been implied of differences between diagnostic groups in terms of measures of construing is inconsistent with results in three major respects.

(i) Schizophrenics do not appear to be a homogeneous group. Thought-disordered schizophrenics behave in relation to the Intensity and Consistency of Relationship measures as predicted and thereby are significantly differentiated from non-thought-disordered schizophrenics and other groups. On the other two measures although thought-disordered and non-thought-disordered schizophrenics are not significantly differentiated they do have other groups occurring on the continua between them.

(ii) Depressives and Neurotics do not appear as a single group on any measure and Depressives appear distinct from all other groups on the Coefficient of Variation measure. The argument used to support the original hypothesis that schizophrenics would have significantly high variability may well have been at fault in relation to thought-disordered schizophrenics at least in that this group has construct relationships which have weakened to their asymptote thus manifesting very low variability. In terms of construct theory and what is known of the Depressive diagnostic group the present author can advance no explanation which would account for the singular position of depressives on the Coefficient of Variation measure.

(iii) While neurotics tended to have the position above normals which was predicted for them, they were not significantly differentiated from normals. The Social Deviation measure is in general a poor discriminator and although Non-thought-disordered schizophrenics are differentiated from Normals by

their social deviation scores, there is no evidence that all psychological abnormalities as such are necessarily associated with a *socially deviant* pattern of construct relationships.

With regard to the value of the approach as a whole, since Kelly argued that behaviour is a function of construing it could be inferred from this that groups categorized for broad behavioural differences (psychiatric diagnoses) would show differences on measures of construing. Kelly also argued that major aspects of construing could be measured by using techniques derived from the matrix of constructs (the repertory grid) suggested by the theoretical concept of "constructs". From this position it could be argued that if the construing patterns of a number of groups broadly differing in behaviour were measured, then a number of significant differences in various aspects of construing would appear between the groups. In general, this expectation is borne out. Moreover, within the limits of the single experiment and accepting the need for replication, the results suggest that it is possible operationally to define schizophrenic thought-disorder in terms of weakened construct relationships as measured by this form of repertory grid technique, and indicate that this phenomenon could be isolated both between diagnostic categories and within the overall category of schizophrenia.

It must be stressed that although significant differences were manifest in terms of broad diagnostic labels and in terms of the phenomenon of "thought-disorder" the measures did not relate significantly (nor where relations predicted) with other psychiatric classifications of schizophrenics such as the classic paranoid-catatonic-hebephrenic-simple groupings.

It should be noted with regard to the question of the independence of the various measures derived from the form of repertory grid test used that the measures Consistency of Relationship and Intensity of Relationship correlate positively for all groups (Spearman's rho) with a mean correlation of $+0.630$. No other pair of measures show consistent direction of correlations over the five groups so that it appears, in practice, that there are three clearly independent measures within the four cited. However, it should be noted that although the two measures mentioned correlate significantly, the discrimination they give between thought-disordered schizophrenics and members of other groups is *improved* when they are added together, thus the discriminating variance of the two measures may not be entirely held in common.

SUB-EXPERIMENT

In order briefly to examine the relationship between construct matching scores (as defined in the main experiment reported) and what is popularly meant by "meaning" the following experiment was carried out. Ten normal subjects (a different group from the one used in the main experiment) were given the ten terms used in the main experiment and asked under each term to list the other nine as follows: "Put first the one nearest in *meaning* to the heading term, then the second nearest in *meaning*, working down to putting finally the one which is most opposed in meaning". Thus each subject presented 10 rankings, one for each term and there being ten subjects there was a total of 100 rankings. The terms were then ranked according to the order indicated by the mean matching scores of the 20 normal subjects of the main experiment. Thus under "LIKEABLE" was placed the term with the highest positive matching score (i.e. GOOD) then the term with the next highest positive matching score (i.e. SINCERE) down to the term with the highest negative matching score (i.e.

PREJUDICED); similarly for each of the ten terms. It was then possible to run rank order correlations between each list of terms as ranked by test quantification and as ranked by each of the ten normal subjects instructed to order by "meaning". "One tail" tests of significance were used since a positive correlation would always be predicted. Using the levels of significance for rank order correlations given by Siegel (1956) the results of this sub-experiment are given in Table VIII.

TABLE VIII

Positively significant at 1 per cent. level	..	..	..	..	..	..	54
Positively significant at 5 per cent. level	..	..	..	..	..	..	30
Positive but not significant	..	..	..	..	..	..	13
Negative but not significant	..	..	..	..	..	..	2
Negatively significant at 5 per cent. level	..	..	..	..	..	..	1

The implication is clearly that a construct relationship (as operationally defined in terms of matching scores) is akin to "meaning" and the relationship of this measure of meaning to Osgood's (1957) semantic differential in likewise manifesting an overall GOOD-BAD "factor" is discussed in Bannister (1959).

THE SCHIZOPHRENIC PROCESS

Current theories concerned with schizophrenic thought-disorder were adversely criticized on the grounds that they are purely *descriptive* and do not suggest a mechanism for the condition which they describe. If we accept for the sake of argument that weak construct relationships in the sense in which they have been here experimentally demonstrated are central to schizophrenic thought-disorder, then we can refer to construct theory as a whole for possible hypotheses concerning process. The line of thought which immediately suggests itself hinges on the idea that changes in construct systems are related to their validation history. For example, if the construing of a person as "loving" is invalidated, then the tendency may be to construe the person in the contrast pole as "hating", but the acquaintance may then exhibit behaviour more appropriate to the "loving" pole and we may duly shuffle him back to be construed under that pole. However, if invalidation occurs in this manner repeatedly, the tendency may be to regard the construct as in itself inadequate to subsume the elements (behaviour of the acquaintance) under consideration and may itself be, in some way, modified. This modification could take the form of loosening the construct, that is to say, weakening its relationships with other constructs, so that it leads to varying predictions (the definition of a loose construct). Thus *loosely* to construe a person as "loving" would *not* be automatically to anticipate from him "sincere" and "likeable" and so on behaviour, since the relationships between the constructs normally constellated with "loving" have been weakened. In this way, the construct would be damaged as a predictive instrument since it would lead to varying predictions but it would be strengthened as an explanatory instrument, since *post hoc* it would be capable of covering events.

Naturally this type of explanation would have to be elaborated to account for interaction effects once parts of a construct system had become weakened and to set up parameters for the change process as a whole. However, construct theory does appear to contain the postulates and terminology necessary for this kind of causal analysis and since invalidation could be produced in a laboratory setting and since in repertory grid techniques we have an instrument

potentially capable of measuring construct changes of various kinds, then hypotheses set up from this source should prove testable.

The Clinical Signs of Schizophrenic Thought-Disorder

The characteristics of the talk of thought-disordered schizophrenics which gave rise to the psychiatric concept of thought-disorder in schizophrenia, have already been given in the terms used by Mayer-Gross, Slater and Roth (1954). In terms of loosened construing, as defined in the present work, can these particular characteristics be at all accounted for?

(a) The first characteristic is "inconsequential following of side issues". As has already been pointed out, the whole idea of relevance seems to be related to the idea of structure and relationships in constructs; if we are talking about politics then we utilize the whole construct sub-system which we have developed to subsume elements normally thought of as political. If relationships between constructs and between construct sub-systems have been loosened, i.e. weakened, then the *focusing* and *restricting* effect of the construct sub-systems will be lost and incidental features of construct symbols may lead us out of the field altogether.

(b) The second two characteristics particularized were tendencies for the thought to be directed by alliterations, analogies, clang associations, associations with accidents of the speaker's environment, symbolic meanings and the condensation of several (perhaps mutually contradictory) ideas into one and the use of words out of context. It can be generally argued that construct relationships are in fact what we usually refer to under the term "meaning" and tentative experimental validation has been given for this assumption. If, therefore, construct relationships are weakened, there is, *ipso facto*, a weakening in meaning. Normally, our talk is firmly *anchored* in the meaning of terms but if meaning grows weak, then other more or less meaningful aspects of terms may begin to guide our talk. Clang associations, condensations and so forth, become important and begin to affect tenor and direction of thought, precisely because the *anchoring effect* of strong meanings is lost.

(c) The characteristic of "clinging to unimportant detail" is particularly interesting, since it obviously implies "important in normal thinking". The importance of details is a function of the superordinacy in the hierarchy of the personal construct system of the particular constructs which normally subsume them. If a person's construct system has loosened, then subordinate/superordinate relationships between constructs may have altered in direction, or at least been proportionately minimized. Thus, in the eyes of the schizophrenic, he is obviously not "clinging to unimportant detail" but persevering with a consideration of some aspect which, within his loosened frame of reference, now occupies a relatively superordinate position.

(d) The next two characteristics both refer to vagueness and poverty of ideas, features which seem consistent with the idea of loosened construing. Again, if we construe loosening as "loss of meaning" then the rich and intricate pattern of significance produced from a complex and structured network of constructs will disappear under loosening and something more nearly approaching noise in the guise of verbal symbols may result.

(e) Finally, indications of thought blocking and indications of pressure of thoughts are judged to be characteristic of the talk of thought-disordered schizophrenics. At a lower level of abstraction this could be described as a

tendency to produce either unusually rapid talk or talk marked by pauses more frequent and longer than is usual. To explain this abnormality we must first consider what governs the rate of production of talk in normals. If we consider talking and by inference thinking, to be a process of *serial construing*, then at the end of each "unit of construction" a person is faced with a related network of constructs, relevant because they are structurally related, which he must *scan* in order to select the next "unit of construction". It is the existence of this related network of constructs which regulates speed of talk and thinking, both insofar as the relationships ensure that further channels for construing are available, thereby facilitating continuance, and insofar as there is a network of relationships and not a single continuous line, thereby setting up optimal speeds of talk by presenting a sequence of *multiple choice* situations. Once construing is loosened, as for the thought-disordered schizophrenic, the optimal and minimal speeds of construing are widened and greater variability can be anticipated. This because the weakening at a certain level may reduce the number of related constructs and thereby reduce the number of items in each multiple choice situation, thus facilitating more rapid talk. At more severe levels of weakening by loosening, constructs may be produced which relate to virtually *no others*, thereby presenting not a reduced choice of channels, but no channels whatsoever, with consequent blocking.

This type of explanation designed to account for the specific characteristics of talk in thought-disordered schizophrenics has, perhaps, little heuristic value without operational definitions and experimental realization but it seems necessary to indicate that there are no obvious contradictions between the phenomena of thought-disordered talk as it presents itself and the explanation in construct terms given for the schizoid condition as a whole.

CONCLUSIONS

In the experiments described the explanatory concepts and the techniques were deliberately stretched to their limit for "pilot" purposes and until the work is replicated and extended, conclusions can only be of a most tentative kind. However, three possibilities seem worthy of further examination:

- (i) That personal construct theory may prove a useful orientation for experimental work in psychology.
- (ii) That repertory grid techniques may provide a useful mode of investigating aspects of conceptual relationships.
- (iii) That weakening of construct relationships as defined in the work reported, may be a useful explanatory starting point for an attack on the clinically observed phenomenon of schizophrenic thought-disorder.

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PURINES IN THE URINE OF NORMAL AND SCHIZOPHRENIC SUBJECTS

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ALTHOUGH there have been many attempts to discover in the body fluids, chemical peculiarities characteristic of schizophrenic illness, the outcome of most of these investigations has been inconclusive (see for example Altschule, 1953; Kety, 1959). Little attention has been paid, however, to purine metabolism until the recent studies of Kishimoto (1958) who reported peculiarities in the absorption spectra of body fluids in schizophrenia which he attributed to abnormalities in the conversion of adenine through hypoxanthine and xanthine to uric acid. These findings appeared to be supported by evidence which included the determination of urinary xanthine by a xanthine oxidase method based on that of Williams (1950).

Recent development of alternative methods of analysis for urinary purines has offered the opportunity of appraising these findings. Adenine, xanthine and hypoxanthine are excreted in quantities of only a few mg. per day, and only recently have methods developed by Weissmann, Bromberg and Gutman (1957) and Weissman and Gutman (1957) been available for their determination in less than a day's output of urine. Weissman's methods are largely chromatographic, and are well documented; they apply to the purines named and to several others. It was therefore considered of value to adapt his methods for repetitive determinations in groups of subjects available to us, so that information could be obtained on these matters and so that the suggestions of Kishimoto could be examined at the same time by an independent method.

It was also considered important, in view of the notorious difficulties associated with the clinical problems of schizophrenia, to attempt to minimize some of the more obvious experimental complexities. For this reason particular care was devoted to the selection of cases. A matching procedure was introduced which took into account the subject's age, sex, weight and nutrition.

METHODS

CLINICAL

The urinary purines were determined in a series of schizophrenic in-patients at the Bethlem Royal and the Maudsley Hospitals (case histories are appended), and in a matched series of normal subjects. The diagnosis was based on classical

data laid down by Bleuler, i.e. thought-disorder of a characteristic type with disturbance of volition and affect; in addition the presence of primary delusions was accepted as strongly suggestive of the illness. In the selection of schizophrenic patients an endeavour was made to obtain cases in the younger age groups with short histories and severe symptoms. The patients had all been labelled as suffering from unequivocal schizophrenia by physicians responsible for their care. As a further precaution two of the authors (R.C. and M.S.) made independent assessments of the clinical features at separate diagnostic interviews. A four-point rating scale was employed and only when both observers regarded each patient as falling within the two most abnormal categories was the patient accepted for investigation. Drug treatment was suspended a few days before testing except when such an interruption in therapy appeared likely to affect the patient's condition adversely.

Case 1

Mr. D.P., aged 30, was admitted to the Maudsley Hospital on 5 August, 1958.

There was no family history of mental aberration apart from a transient depressive illness which an older sister had developed at the age of 40.

The patient had developed normally and had made average progress at school. On leaving school he took up bricklaying for 4 years, served with the army in Egypt for 2 years and then worked as a lathe setter for 8 years until the onset of mental symptoms when he lost his job.

He had married happily at the age of 22 years; his wife was 3 years older than he; they had two healthy children.

The patient was described by his wife as having been a good mixer, not given to fits of depression. He was generally easy-going, quiet and methodical. His leisure interests had been mainly sporting.

Eighteen months before admission the patient began to interest himself in politics and simultaneously he neglected his other pursuits. He gave up all his usual activities and neglected his appearance. A few months later he suddenly became unreasonably anxious and complained of depression and insomnia. He was admitted to a mental hospital where he was given first E.C.T. without effect and then received 44 insulin comas, after which he seemed a little better. Eventually he took his own discharge.

Following his discharge he was unable to work; he felt depressed and complained of an inability to think clearly. He also told his wife that he could not control his thoughts and that he could hear voices inside his head repeating advice which he had been given in the past, e.g. "walk, watch and listen". He spent his time unoccupied at home before his admission.

On examination he was noted to be a burly, plethoric man in satisfactory physical health apart from a moderate hypertension. He was rather hostile to the examining doctor and made occasional odd grimaces and gestures. Several times he burst into tears for no reason. He seemed to have difficulty in expressing himself in speech and the meaning of his statements was often difficult to grasp. He stated that he had voices in his mind repeating instructions and that he felt as if he were thinking what others were thinking. He also complained that when addressed he seemed to visualize all subjects of conversation.

The administration of reserpine 3 mg. t.d.s. resulted in an improvement of his over-activity; it had, however, produced little effect on his mental state at the time of examination.

Case 2

Mr. K.W., aged 25, was admitted to the Maudsley Hospital on 24 June, 1958 on account of disturbed behaviour at home.

The family history was negative apart from psoriasis among some of his father's relatives.

The patient was born in Wales. His early development was normal. He was an average scholar and left school at the age of 16 years. He then took four short office jobs before entering the army for his National Service at the age of 18 years. In the army he frequently overstayed his leave and absconded several times. After making a suicidal attempt following the death of his father he was kept in detention for 6 months before his discharge from the service. During the following year he held three jobs briefly as an office filing clerk. At the age of 21 he developed a psoriatic rash over his scalp and forearms which subsequently spread all over his body.

Before his illness he had been cheerful and popular but sensitive to the opinions of others. He tended to be egocentric and he daydreamed to an unusual degree.

His illness began about 2 years before his admission, when he gave up attempts to find work. He claimed that if it had not been for his skin condition he would have found work though the rash was in reality not very severe. Four months before admission he attempted suicide with coal gas and his behaviour deteriorated subsequently. He became aggressive

towards his mother and refused to talk to her. During angry outbursts he smashed door panels and broke chains. He said that he could hear the voices of a lady who told him to pray for forgiveness and of a man who encouraged suicide. On several occasions he complained of having a woman inside him and of having his genitalia manipulated by a hypnotist. He often smiled and laughed to himself for hours and said it was difficult to think straight. Many times he exposed himself to his mother and masturbated.

On examination after admission he was noted to have a mild generalized psoriatic eruption. Mentally he was well behaved and smiled fatuously all the time. There was considerable flattening of affect as well as thought blocking and concreteness of thinking. Although his intelligence was average on formal testing he had difficulty in interpreting proverbs. He did not regard himself as ill and thought that anyone with psoriasis would behave as he had done. He was tested before drug-treatment was commenced.

Case 3

Mr. E.S., aged 35, was admitted to the Maudsley Hospital on 26 June, 1959.

There was no family history of mental disorder. The patient had developed normally and had made average progress at school. On leaving school at the age of 14 years he took unskilled jobs for 3 years until he was called up for the army in 1939. He served for 7 years and reached the rank of lance-corporal. After demobilization he worked as a cleaner, his longest spell at one job being 7 years.

He was married at the age of 26 years to a typist after an acquaintanceship of 6 months. The marriage was never harmonious; there were frequent quarrels over the upbringing of their two children. His wife was a perfectionist who insisted on unattainable standards of tidiness in the house.

Before the onset of his illness the patient was a rather quiet, moody, hard-working man with few friends. He was quick-tempered and careless over details. His main interests were in football pools and the cinema.

The illness was very gradual in onset. In 1953 he changed from day to night duty in order to observe his wife's handling of the children as he felt that she had been mismanaging them. In 1954 he left his job because of a quarrel with his supervisor and then became increasingly moody and subject to fits of temper. In 1956 he became sexually demanding and 6 months before his admission he complained of sabotage at his place of work and of an organized plot directed against him. He maintained that his workmate was mentally defective and that newspaper articles bore a special reference to him. Eventually he claimed that his workmates had been sent from the law courts to observe him and he became so distressed that it was necessary to summon the duly authorized officer.

On examination in hospital he was in good physical health. He was in a state of mild agitation and very suspicious of the staff and other patients. He demonstrated marked thought-disorder. Innocent remarks and gestures by other patients seemed to carry sinister meanings and he thought that certain television programmes referred to him. He was receiving chlorpromazine 150 mg. t.d.s. at the time of testing.

Case 4

Mr. N.O., aged 22 years, was admitted to the Maudsley Hospital on 2 May, 1959 from an observation ward.

There was no family history of mental illness. His father was an Italian waiter and his mother was of English stock. He was an only child.

His early development was unremarkable and he did well at school, both scholastically and socially. On leaving his grammar school he obtained a scholarship to an art school where he made good progress at first. His military service was deferred to enable him to complete his studies.

Before his illness he had been cheerful, stable and confident, with a few close friends of his own sex and many superficial acquaintances. He took a keen interest in art and philosophy.

Seven months before admission he became increasingly solitary, lost interest in painting and stayed away from art school. He daydreamed a lot at home and ate very little. He said that he could see a cross in the sky and he felt compelled to pray continuously and also to fast because, he maintained, Jesus Christ had done so. It was his stubborn refusal to eat which led to his admission to the observation ward.

On admission to hospital he was in good physical health. His psychomotor expression was restricted and his affective responses were flattened. His talk was rambling and imprecise and its meaning was uncertain. He spoke of "visual voices" which he defined as the voices of people whom he could see. He complained of feeling "out of tune" and stated that this feeling was related to "changing colours as the clouds pass over the sun . . . it takes the character of a moment". He was unable to interpret proverbs, tending to respond with another proverb. One month after admission insulin coma treatment was commenced but he refused further treatment after the first coma. He then began to talk of hearing the voices of a brother and sister in his thoughts. He was not receiving drugs at the time of testing.

Case 5

Mr. F.H., aged 17, was admitted to the Maudsley Hospital on 2 February, 1959 from a local general hospital to which he had been sent by his own doctor.

His mother, a German Jewess, had been in a mental hospital for some years for an illness which had been diagnosed as paranoid schizophrenia. The patient was reared by his father on account of his mother's illness. His father died early in 1958.

The patient's early development and school career were normal. On leaving school at the age of 16 years he began work as a shipping clerk, taking night-classes in shorthand and French.

He was described by his guardian as being normally a confident but sensitive youth with few close friends. He was shy with girls but at ease with older people. He tended to daydream.

During his last few months at school he had become increasingly shy and sensitive; his standard of school-work deteriorated and he obtained surprisingly low marks in the G.C.E. After beginning work he developed numerous hypochondriacal complaints and then accused his guardian's wife of organizing campaigns against him.

On examination he was a small, pale youth with cold blue hands. His talk was slow but normal in form. He complained of a fog over his mind and wondered whether he needed a brain operation as he could feel a tight band around his head which was making his head large and his body small. He also feared that he might be changing his sex. His mood was one of perplexity and apprehension. He attributed his morbid experiences to the efforts he had made to avoid accusing his aunt of starting campaigns against him. He was given 46 insulin comas without demonstrable effect. He was not under any drug treatment at the time of testing.

Case 6

Miss E.P., aged 23, was admitted to Bethlem Royal Hospital on 13 December, 1958.

The patient and her identical twin sister were adopted soon after birth by a well-to-do elderly couple and no information was available about the mental health of her true parents.

Her early development was slow and she was a difficult child with frequent temper tantrums and night terrors. At school she did poorly; during her final year she became a prefect for a time but was demoted the following term on account of her unkindness to younger girls.

Her periods were always painful and irregular. She had some homosexual inclinations in adolescence but never displayed heterosexual interests.

Prior to her illness she had been a shy, brusque, jealous girl lacking in self-confidence. She was affectionate towards her adoptive mother but had no close friends. She was a day-dreamer, very interested in ballet, music, plays and fairy tales. She was liable to sudden changes of mood and would sulk and cry for no apparent reason.

Her illness commenced insidiously. At the age of 18 years she started work at a secretarial college but left after 8 months: she found the pace too rapid for her and she was disturbed by homosexual feelings. After an attempt to take a domestic science course she tried several jobs, only to be dismissed each time for incompetence. She became hostile, self-absorbed and negativistic; she thought she might lose her reason. At the age of 20 years she entered a private hospital in Devon but had to be transferred to Bethlem Royal Hospital on 12 January, 1956. At that time she was unkempt, hostile, pouting, solitary and sullen, inclined to scream suddenly at the staff if she were frustrated. Her talk was disjointed with evidence of thought disorder; incongruity of affect was noted. Her attention and concentration were poor; there were no delusions or hallucinations. She was treated with reserpine and her behaviour slowly improved. She ate ravenously and put on much weight. In due course the dosage of the drug was reduced and she was well enough to be discharged 8 months after admission.

Two months later it was necessary to re-admit her as she had become agitated at home; she had accused her adoptive parents of influencing her mind and of working against her. She also stated that another lady aged 90 years was homosexual. Her clinical state was similar to that of her first admission except for her refusal to look at doctors and a determination to sit with her arms folded looking at the floor. She was treated with drugs at different times. Eighteen months after her admission she was sufficiently well to return home and take a typing job.

Five months later she again relapsed and was re-admitted. On this occasion her talk was less coherent than it had been but otherwise the abnormalities of her mental state were not substantially different from those which had been recorded previously at the time of testing.

Case 7

Mrs. E.M., aged 30, was admitted to the Maudsley Hospital on 23 February, 1959 from an observation ward to which she had been taken by the duly authorized officer on account of delusions, hallucinations and agitation at home.

She came from a poor farming family in Southern Ireland. There was no family history of mental illness. Her early development had been normal and she had suffered no significant illness or injury apart from a blow on the head at the age of 7 years, following which she was unconscious for some hours. She had been treated recently for anaemia. She made fair progress at school but left at the age of 12. She had won a competition as a beauty queen in Ireland. She married at the age of 20 years and two years later came to England where her husband obtained work in an iron foundry.

During the 7 years before her admission she had given birth to 7 sons and each pregnancy had been marred by severe vomiting in the first trimester. Following the last delivery 2 years before admission she was said by the nurses to be "hysterical". Her husband described her

as being normally somewhat moody, withdrawn and irritable; she was always considered "different" by her family. She had been a devout Roman Catholic until 3 years before her admission and had always been superstitious.

Shortly after her marriage while working as an usherette in a cinema she complained that men were following her but she produced no evidence to support her accusations. Her husband dated the onset of her illness to 5 years before admission when she expressed the persistent, irrational belief that her sister-in-law had dyed her child's hair. Three years before admission she ceased attendance at mass and expressed bizarre ideas about science. She complained bitterly about her living conditions. She became more preoccupied, withdrawn and suspicious and 2 months before admission began to scream at the window, apparently in answer to hallucinatory voices. She continued to deteriorate until her husband was obliged to call the duly authorized officer.

On admission she was physically well but was withdrawn, suspicious and obviously hallucinated. Her talk was barely coherent and was broken by frequent silences. As she spoke she made praying gestures with her hands and at times she looked into one corner of the room and whispered. She expressed delusions that her body was changing, that she was being deprived of her thoughts, that her family had been killed and that her food was poisoned. As she discussed her symptoms she smiled and giggled to herself. Asked to interpret the proverb "A stitch in time saves nine" she laughed and said "... that means if you stitch your clothes some of them are more holy than God". She was examined in this condition.

Case 8

Miss B.C., aged 25, was transferred to the Maudsley Hospital on 10 July, 1959 from an observation ward to which she had been admitted one week earlier.

There was no family history of mental illness. The patient's development and school record had been unremarkable apart from attacks of bad temper as a child. From 17-22 years she had helped on her parents' poultry farm near Oxford. She then went to live for 18 months as the mistress of a man whom she had met on holiday at Torquay. At the age of 24 years she took a post as assistant matron at a boys' grammar school from which she was dismissed 2 months later (on 2 March, 1959) on grounds of unsuitability.

She had suffered no serious physical illness. Her previous personality had been marked by moodiness, short-lived depressive spells and a preference for her own company.

After her dismissal from the grammar school she took a train to London without a ticket saying that she was going to see her royal parents at Buckingham Palace and that she had been told to do this by voices. The station authorities summoned the duly authorized officer who transferred her to the observation ward.

On examination her extremities were noted to be cold but her physical health was otherwise satisfactory. Her speech was slow, vague in content and accompanied by incongruous smiles and laughter. She complained of feeling sad and strange and objected to seeing the name "Miss King" on the end of another patient's bed as she regarded this as an insult to her father.

She was given chlorpromazine 50 mg. t.d.s. with little effect on her mental state by the time she was examined.

Case 9

Mrs. H.S., aged 48, was admitted to the Maudsley Hospital on 27 July, 1959 from an observation ward.

She had been brought up in Wales, the seventh child of a family of nine, most of whom were illiterate. There was no family history of mental illness.

Her development was normal but she was a poor scholar. After leaving school at the age of 12 years she came to London as a domestic and had several short-lived jobs in the first few years.

She married at the age of 18 years in 1928, having known her husband for 2 years. He was only one year older than she but he remained unemployed until 1940 when he joined the army. The marriage was unhappy but they had 8 healthy children before separating in 1951. She had never wished her children to go to school and in consequence they had acquired little education. Two years before her admission the patient lived with another man who described her as being cheerful, argumentative and rather suspicious. She did her housework well but associated very little with other people as she felt they were always talking about her.

For about 25 years the patient had entertained the beliefs that she was Queen of England and that other people living above her in her home were trying to poison her. During the year before admission she expressed such notions more frequently. One day without warning she travelled from Wales to London where she was found by the police outside Buckingham Palace proclaiming herself to be Queen.

On admission to hospital she was in satisfactory physical health. Mentally she was co-operative and fairly sociable. She was correctly orientated and answered questions not related to her illness rationally and coherently. Her mood was cheerful but she became angry on seeing a photograph of the Queen, declaring that the person in the photograph was an imposter. She admitted to constant auditory hallucinations of confused talking and referred to "him up there", pointing to the ceiling. She stated that she owned the hospital and could move about as she liked. She thought her son might have changed his sex. Although stelazine 5 mg.

t.d.s. was prescribed she usually refused medication and her mental state was unchanged at the time of testing.

Case 10

Miss M.H., aged 28 years, was transferred on 27 July, 1959 to the Maudsley Hospital from an observation ward to which she had been admitted 9 days previously.

There was no family history of mental illness. Both parents were stable, intelligent people; the father was a journalist employed by Reuter in South Africa.

The patient was born in London and educated in residential convent schools as her family were often overseas. She matriculated at the age of 15 and undertook secretarial work until she was 21 years; she then studied for 6 months at the Sorbonne and worked as a translating secretary in South Africa for the next 7 years. She returned to England in 1957 and worked with the French Press Agency until her illness.

Before her illness she was regarded as a shy, nervous girl, a strict Roman Catholic who was attached to her family and who had few friends. She appeared to be without heterosexual interests.

She had suffered a previous illness 18 months before admission when she had been admitted to the Bethlem Royal Hospital where her affect was regarded as incongruous and her talk was noted to have been vague and incoherent. She had also displayed various bizarre, hypochondriacal delusions and believed there was something she could not describe growing in her rectum. She was treated with 21 insulin comas followed by a short course of chlorpromazine and seemed to make a full recovery. She had then gone to live with an aunt and she continued with her secretarial work.

Ten months after her discharge the patient asked her employer for a rise in salary. When this was refused she left her job and took a secretarial post elsewhere. Two weeks later she felt that the other people in the office were laughing at her and making suggestive remarks. On 15 June, 1959 she told her friends that she had appeared on television and that she was a medium. Three days later she set out to see her doctor but deliberately allowed herself to be accosted by an Indian; she felt that she had to permit this action as a gesture of atonement but became frightened and struck the man with an umbrella. She was found by the police and taken to an observation ward.

On admission she was in good physical health. Her talk was normal in flow and form but she stated her belief that her mind was being shared by somebody else and that people could read her thoughts at a distance. She also felt that the nurses were observing her for lesbian tendencies and that an outside agency was placing abusive words in her mind.

She was treated with stelazine 5 mg. t.d.s. and was improving at the time of testing.

The control series consisted of members of the staff of the Institute and the Joint Hospitals, matched with the patients in age, sex, weight and height. The degree of matching can be judged from Tables IX and X. The subjects were all ambulant during the experimental period and continued with their normal diet. In addition all caffeine-containing drinks, e.g. tea and coffee, were recorded in every case and note was taken of any special features of eating, drinking and behaviour during the test period. Since both staff and patients received some of their meals from the same kitchen the diets overlapped to some extent. From each subject an accurate 24-hour specimen of urine was collected in a large polythene bottle containing 10 ml. of chloroform as preservative. Nurses supervised collections made by patients. In a number of cases further 24-hour specimens were obtained from the same patient so that variations in urine output, their diet and changes in drug treatment were examined.

DETERMINATION OF URINARY PURINES

The methods of Weissmann *et al.* (1957) were applied, modified as detailed below for repetitive determinations with 1/10 of the daily output of urine. The methods involve removing the bulk of the uric acid from a fraction of a day's excretion, by keeping cold with acid; adsorption of the purines to a Dowex resin and their elution with ammonia; their precipitation with silver salts and separation by paper chromatography. On the paper, purine spots are identified in ultra-violet light, eluted individually, and measured spectrophotometrically.

The 24-hour specimens of urine were taken to pH 2 with 2 N-HCl (short range indicator paper), kept at 4; C. for 16 hours or longer, filtered through

fluted papers, and 1/10th of each specimen used for each determination. Determinations were carried out in duplicate, and in addition urine equivalent to a further 1/5th of the specimen was kept at -25°C . for future use.

(1) Adsorption

For adsorption, Dowex 50-H⁺, 8 per cent. cross-linked, mesh 20-50 or 50-100 was used in columns of length 21 cm. and diameter 2 cm., requiring about 50 ml. of resin. Columns were prepared by washing with (a) 50 ml. 2N-NaOH, (b) water until neutral, (c) 100 ml. 2N-HCl and (d) water again until neutral to short range indicator paper. The cycle (a) to (d) was repeated. The washings were discarded.

As the quantity and particle-size of the resin differed from that previously employed by Weissmann *et al.* (1957), a trial experiment was necessary to determine volume of 1 N-NH₄-OH for complete elution. For this purpose 1/10th of a 24-hour urine specimen was dripped slowly for 1 hour through a column of the Dowex 50-H⁺ resin in 50-100 mesh size and the column washed with 250 ml. water. (On some occasions the same resin in 20-50 mesh size was employed: see below.) Fractions of 2.5 ml. were collected from the column by eluting with 200 ml. 1 N-NH₄-OH, followed by 50 ml. water. Optical density of the eluates at 260 m μ was determined after suitable dilution with water and acidification, with 1 N-HCl. A large increase in optical density occurred in specimens collected after about 100 ml. NH₄OH had passed, and was maintained until about 140 ml. were collected (Fig. 1); it was about coincident with the appearance of a yellow colour from the urine. On this basis the standard procedure adopted was to pass the material from 1/10th of a 24-hour collection of urine through the column described, at the rate of 150 ml./hour, followed by 200 ml. of water. The effluents were discarded and the purines eluted with 200 ml. of N-NH₄OH followed by 50 ml. of water; to ensure that minor constituents were not lost, these two effluents were combined and used in the following stage.

(2) Silver Salt Precipitation

The samples after elution were reduced in volume to 3 ml. or less with a rotary evaporator at 20 mm. Hg in a bath at 55° , and pipetted into tubes previously calibrated at 10 and 20 ml. The solutions were taken to pH 2 with N-H₂SO₄ and 2 ml. N-AgNO₃ added, the final volume being adjusted to 10 ml. with water. Tubes were left for 24 hours at room temperature in the dark and for a further 48 hours at 0° . They were then centrifuged (1,500 g.) and the supernatant removed. The silver precipitates were carefully washed with 5 ml. portions of water until the supernatant became colourless (2 or 3 washings). The purine-silver complexes were decomposed by adding 20 ml. hot 0.05 N-HCl and heating 5 minutes on a boiling water bath. The tubes were centrifuged as before and the supernatant retained. The precipitates were washed with further quantities of 10 ml. 0.05 N-HCl. The combined washings or aliquots from them were concentrated to dryness in a round-bottomed flask in vacuum, and any remainder not immediately used was stored at -25° .

(3) Paper Chromatography

The procedure recommended by Weissmann *et al.* (1957) was adopted for two-dimensional chromatography, the concentrate being applied by 3 successive additions of 20 μ l. with calibrated capillary pipettes. The first run was with a

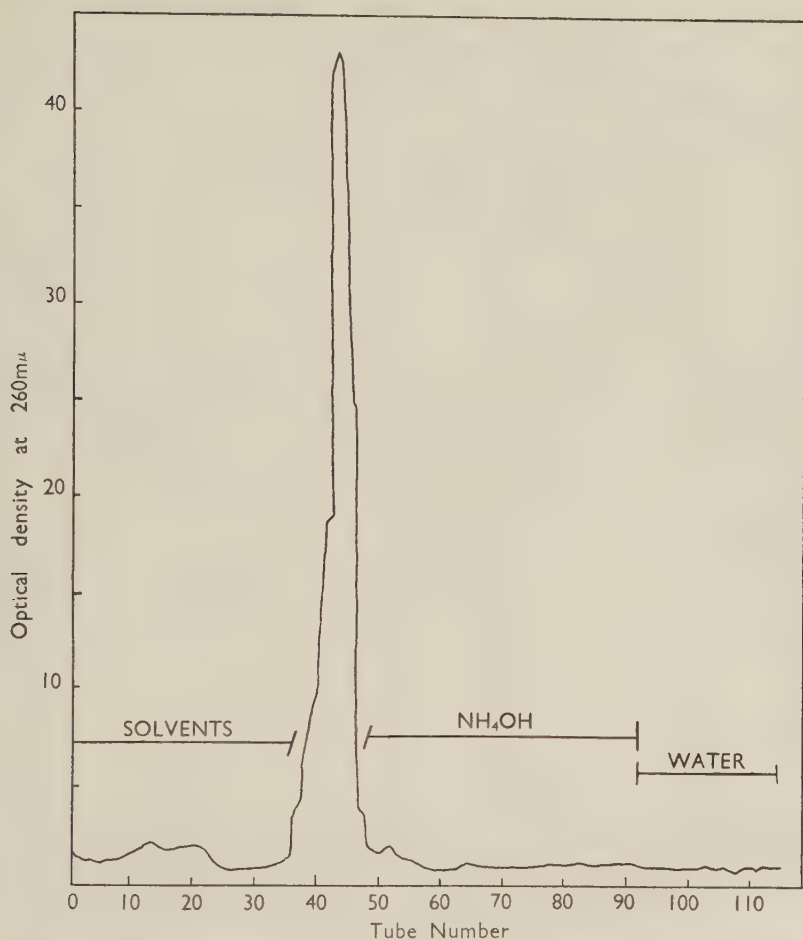


FIG. 1.—Purine analysis: Elution from a column of Dowex —50 H⁺. Urine, water, 200 ml. $\underline{\underline{N}}\text{-NH}_4\text{OH}$ and 50 ml. water were passed through the column as described in the text. The effluents were collected in 2.5 ml. portions in separate tubes, and the optical densities of these samples determined directly or after appropriate dilution.

mixture of n-butyl alcohol (Hopkins and Williams, chromatographic grade) and 0.6 $\underline{\underline{N}}\text{-NH}_4\text{OH}$ (6:1, v/v), for approximately 48 hours. After drying for 24 hours in a stream of air at room temperature the papers were run in a direction at right angles to the previous run, with a freshly prepared mixture of n-butyl alcohol, formic acid and water (77; 11:12 v/v). Spots were located by ultra-violet light with a Hanovia lamp with its main emission at 253.7 m μ . For identification, other sheets were run in the same tanks with known quantities of authentic specimens of adenine, guanine, hypoxanthine and xanthine. Later there was found to be sufficient internal evidence for identification of spots with urine specimens alone (Fig. 2). Adenine was always the fast-moving spot in the butanol-ammonia solvent. Guanine which only occurred in trace amounts and the 1-methyl and 7-methyl guanines which run as one spot, exhibited a strong blue fluorescence when papers still moist from the second solvent system were irradiated by ultra-violet light. Hypoxanthine ran nearly parallel with the latter spot in this solvent but more rapidly in butanol-formic acid (Fig. 2).

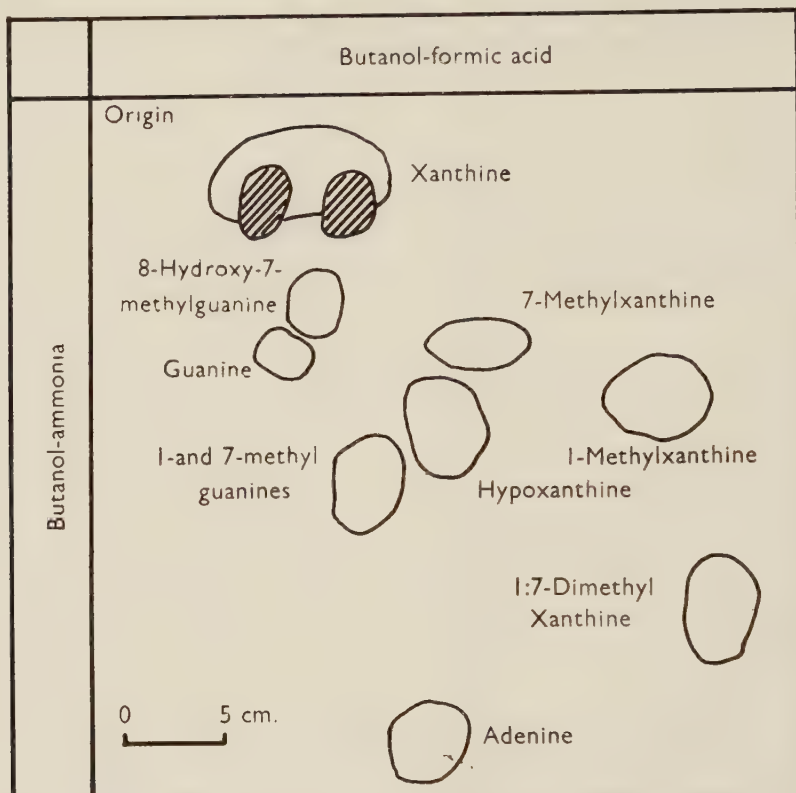


FIG. 2.—Purine-like materials obtained using the standard procedures described under Methods. Materials underlined were those employed as markers for the identification and location of other purines. 7-Methylxanthine, 1-methylxanthine and paraxanthine were from dietary sources. Certain fluorescent materials associated with xanthine are indicated with hatching. The origin is marked by (O) in the upper left-hand corner.

Xanthine as noted remained nearer the origin and was always associated with two characteristic fluorescent spots. Other spots were located in relation to those already mentioned.

(4) Elution Technique

Spots located by ultra-violet light were cut out, and neighbouring areas of the chromatogram of the same size but free from obvious absorption and fluorescence were also taken to act as controls. The papers were cut into pieces 0.5 cm. square or smaller, placed into tubes with 3.5 or 7 ml. water, and macerated. After 15 minutes the suspension was filtered by suction through a small glass funnel through the stem of which was placed a small pointed glass rod, with flattened end above which carried a filter paper about 6 mm. in diameter. The conditions of elution were based on trials in which 25 μ g of hypoxanthine, xanthine, adenine and guanine were extracted with different volumes of solvent for times of 15 minutes to 16 hours, with results shown in Tables I and II. Elution with water proved to be rapid and complete (Table I). In initial trials the four bases were eluted with 3.5 ml. of water, with results (Table I) indicating that 15 minutes was adequate for elution. It will be noted from Table II that the extracts from control areas of paper, obtained under

TABLE I
Recovery of Purines from Chromatographic Procedures
Yield on Elution with Water for

Compound Placed on Paper (μ g)		15 Minutes			16 Hours		
		1st 3.5 ml. (μ g)	2nd 3.5 ml. (μ g)	Total Per cent.	1st 3.5 ml. (μ g)	2nd 3.5 ml. (μ g)	Total Per cent.
Hypoxanthine	25.1	23.2	1.1	97	22.6	1.3	95
Xanthine	20	18.3	1.2	97.5	16.8	1.7	92.5
Adenine	30	27.5	1.6	97	27.5	2.0	89
Guanine	22	19.5	1.4	95	17.5	2.0	89

The purines were applied to a 35 $\times$ 38 cm. sheet of Whatman 3 mm. paper, which was dried and run in butanol-ammonia.

Spots were located and cut out, and control areas of paper taken, as described in the text (see also Table II). A third elution yielded no further absorbing material.

TABLE II
Recovery of Hypoxanthine Standards from Chromatographic Procedures

Hypo- xanthine Added (μ g)	Elution Volume (ml.)	Optical Density of Eluates		Hypoxanthine Recovered	
		Standard	Control	μ g	Per cent.
25.1	3.5	0.564	0.045	23.2	92.5
50.2	3.5	1.064	0.045	45.5	91
25.1	3.5*	0.565	0.060	22.6	90.5
—	3.5†	0.087	0.057	1.3	95.0
25.1	5.0	0.399	0.027	24.0	95.5
50.2	5.0	0.793	0.027	49.0	97.5
25.1	7.0	0.295	0.021	24.6	98.0
50.2	7.0	0.556	0.021	49.0	97.5

Specimens placed on sheets of Whatman 3 mm. paper with the same capillary pipette, volume 20 μ l., and delivery 25.1 $\pm$ 0.2 (3) μ g hypoxanthine (measured directly in 3.5 ml. water). Results are obtained after subtracting values with solutions from control areas of paper. Each value is the mean of duplicate readings agreeing within 5 per cent.

* Elution for 16 hours; others employed 15 minutes elution.

† A second 16-hour elution of sample and control; the per cent. recovery quoted refers to the sum of material from the first and second elutions.

different conditions, did not give the same absorption readings and it was thus necessary to take separate control areas for the different spots. The control values however remained less than 1/10th of those given by the purine-containing areas. In actual determinations in the urine extracts, control values were greater; thus in the experiments of Table V they were approximately 1/5th of values from the purine-rich areas. Elution for longer periods, or repeated extraction, gave increased elution in control papers from areas without purines and is thus undesirable. Results indicate that for spots expected to contain some 50 μ g. of purine, a volume of 7.0 ml. gave recovery of 97 per cent. or more. These recovery values were obtained with hypoxanthine, xanthine, 1-methyl, 7-methyl and 1:7 dimethylxanthine. For spots of some 25 μ g., elution in 3.5 ml. is recommended (Tables II and III).

(5) Spectrophotometric Measurement and Calculation

The eluates were buffered at pH 2.1 by adding 35 μ l. of a solution 0.5 M in HBO_3 , M in Na_2HPO_4 and 2.4 N in HCl, and absorption determined at chosen wavelengths with a Hilger Uvispek instrument. In initial experiments,

the absorption spectra of the materials eluted from urine were measured at a range of wavelengths and at other pH values in order to establish their identity. The findings agreed with those of Weissmann *et al.* (1957) and earlier workers, and accordingly the previously recorded extinction maxima and extinction coefficients were adopted in the observations and calculations of the present study. The values employed are quoted in Table III. The sample applied to the

TABLE III
Photometric Data Employed

Spot	E Maximum (mg./100 ml.)	Absorption Maximum (m μ)
*Hypoxanthine	0.78	248.5
Xanthine	0.64	266
*1-methylguanine with 7-methylguanine	0.62	250
*Adenine	0.93	262
8-hydroxy-7-methylguanine	0.88	248
*Guanine	0.69	248
1-methylxanthine	0.70	266
7-methylxanthine	0.60	268
Paraxanthine	0.53	268

The data is derived from sources indicated by Weissmann *et al.* (1957).

* Areas of paper bearing these compounds were eluted in 3.5 ml. water, and the others in 7 ml.

paper is 60 μ l. of 800 μ l., derived from 1/10th of the 24-hour output of purine; accordingly:

$$\text{Excretion (mg./day)} = \frac{\text{density read}}{E_{\text{max}}} \times \frac{800}{6} \times \frac{3.5}{100}$$

when readings are made with 1 cm. cells, of material eluted in 3.5 ml. (E referring to mg./100 ml.).

(6) *Recovery of Purines Added to Urine: Repetitive Determinations*

Recovery experiments were carried out with guanine, adenine, hypoxanthine and xanthine, added to urine specimens in concentrations comparable with those normally excreted. Application of the full procedure described above showed mean recoveries of hypoxanthine of 97, xanthine of 64, adenine of 79 and guanine of 78 per cent. (Table IV). These were close to recovery values obtained by Weissmann *et al.* (1957) from an artificial mixture containing some constituents of urine.

Consistency of results on repetitive determinations was appraised under the following circumstances: (a) between duplicate determinations carried out with all specimens on the same occasion; (b) between determinations on the same specimens before and after storage; and (c) between different specimens from the same subject voided at different times.

(a) An example of determinations carried out with specimens from one pair of subjects is quoted in Table V, indicating the degree of agreement between the duplicate determinations of each purine normally carried out with all specimens. In the further example of Table VI, four determinations of each purine were carried out and the variation among the results is expressed as

TABLE IV

Recovery of Purines from Urine Specimens

		(a) Purine Output (mg./24 hour)	(b) Purine Added (mg./24 hour specimen)	(c) Purine Found (mg./24 hour specimen)	Difference (c-a)	Recovery (Percentage $\frac{c-a}{b} \times 100$)
Hypoxanthine		6.0	9.0	14.0	8.4	93.5
		5.0	8.4	13.2	8.2	98
		5.4	10.0	14.6	9.2	98
Xanthine	..	5.5	6.8	9.8	4.3	63
		4.8	5.0	7.75	2.95	68.5
		4.2	5.0	7.2	3.0	60
Adenine	..	0.9	3.1	3.6	2.7	87
		1.1	3.0	3.2	2.1	70
		1.0	3.0	3.5	2.4	80
Guanine	..	0.4	2.0	1.9	1.5	75
		0.3	2.1	2.1	1.8	84
		0.2	0.5	0.6	0.4	75

Specimens of purines listed were added together to urine in concentrations approximating to the expected daily excretion. This was carried out with three distinct urine specimens and the results compared to those from similar volumes of urine not receiving the additions.

TABLE V

Determinations Carried Out with Urine Specimens from a Healthy and Mentally-Ill Subject

Measurement	Healthy Male (P.W.)		Patient (F.H.)
Age (years)	..	18	17
Weight (kg.)	..	60.5	50.5
Urine volume (ml.)	..	1,408	805
Urinary creatinine (g./24 hours)	..	1.21	1.15
Daily creatinine (mg./kg.)	..	20	23.5
Purine excretion (mg./24 hours):			
Hypoxanthine	..	9.4, 8.7	6.75, 6.0
Xanthine	..	1.2, 2.3	3.4, 4.5
1- and 7-methylguanines	..	3.1, 3.2	4.54, 4.15
Adenine	..	1.2, 1.04	1.63, 1.62
8-hydroxy-7-methylguanine	..	0.43, 0.45	0.99, 0.99
Guanine	..	0.2	0.2

Neither subject was receiving drugs. Specimens were voided during the same period of 24 hours, and handled together throughout all determinations (e.g. during adsorption, chromatography and elution).

a standard deviation. After determinations had been carried out in duplicate with 20 urine specimens, their consistency was appraised as shown in Table VII. These results, and also those of Table VI, show greatest consistency in the determination of hypoxanthine, followed by xanthine, adenine and 7-methylguanine; values for 8-hydroxyguanine were markedly more variable.

(b) Volumes of urine specimens sufficient for duplicate determination were stored at -18°C ., and purine estimations performed after three months

TABLE VI
Repetitive Determination of Purines from Two Subjects

Determination					Healthy Male (J.B.)	Patient (Mr. O)
Age (years)	..	..	..	..	22	22
Weight (kg.)	..	..	..	..	50	50
Urine volume (ml.)	..	..	..	..	1,630	1,167
Daily creatinine (mg./kg.)	..	..	..	..	31.6	21
Hypoxanthine	..	..	..	..	5.5 5.45	4.7 4.8
					5.75 5.95	3.9 4.36
Mean $\pm$ S.D.	..	..	..	..	5.7 $\pm$ 0.23	4.44 $\pm$ 0.4
Xanthine	..	..	..	..	2.0 2.2	3.95 3.4
					2.54 2.7	2.66 3.3
Mean $\pm$ S.D.	..	..	..	..	2.35 $\pm$ 0.4	3.33 $\pm$ 0.53
7-methylguanine	..	..	..	..	3.55 3.3	2.95 3.15
					3.3 3.9	2.85 2.34
Mean $\pm$ S.D.	..	..	..	..	3.46 $\pm$ 0.32	2.82 $\pm$ 0.42
Adenine	..	..	..	..	1.2 1.3	0.91 0.85
					1.4 1.6	0.54 0.70
Mean $\pm$ S.D.	..	..	..	..	1.37 $\pm$ 0.17	0.75 $\pm$ 0.16
8-hydroxy-7-methylguanine	..	..	..	..	0.2 0.1	0.73 0.83
					0.2 0.3	0.3 0.72
Mean $\pm$ S.D.	..	..	..	..	0.20 $\pm$ 0.08	0.64 $\pm$ 0.23
Guanine	..	..	..	..	>0.2	>0.2

Purine determinations were carried out in two groups, the first as described in Table V and yielding the first two values in each group of four below, and the second group from distinct aliquots run on a subsequent occasion. Other details as in Table V.

Neither subject was receiving drugs.

TABLE VII
Consistency of Purine Determinations

Determination	Difference Between Duplicates (Per cent. of mean value $\pm$ S.D.)
Hypoxanthine	4.5 $\pm$ 3
Xanthine	12 $\pm$ 7
1- and 7-methylguanines	13 $\pm$ 7
Adenine	11 $\pm$ 8
8-hydroxy-7-methylguanine	25 $\pm$ 5.5

Purines analyses were carried out with 20 urine specimens, 10 from healthy subjects (5 males and 5 females) and 10 from patients (5 males and 5 females) yielding duplicate values of which Table V quotes examples. The differences between each pair of duplicates was expressed as a percentage of their mean value, the percentages averaged are here quoted with their standard deviations. Guanine excretion was too small for comparable appraisal.

TABLE VIII
Purines in Urine Specimens Kept For or Voided After Intervals of Some Months

Experiment Subject	1 C.P. (male, healthy)			2 E.S. (male patient)			3 R.C. (male, healthy)			4 E.M. (female, patient)		
	(a)	(b)	(c)	(a)	(b)	(c)	(a)	(b)	(c)	(a)	(b)	(c)
Determination	—	Same specimens after 7 months' storage	—	—	Same specimens after 7 months' storage	—	With drug	Fresh specimen 1 month later	Fresh specimen 7 months after (a); no drug	—	Same specimen after 3 months' storage	Fresh specimen 4 months after (a)
Circumstances of storage or collection of urine	—	—	—	—	—	—	—	—	—	—	—	—
Hypoxanthine	5.0	4.6	—	7.8	6.5	—	4.8	6.9	5.2	3.8	3.45	4.0
Xanthine	1.1	1.2	—	2.0	2.0	—	2.1	4.3	4.0	3.7	3.4	3.9
1- and 7-methyl-guanines	2.4	2.1	—	8.9	7.0	—	3.85	5.2	4.5	2.1	3.0	3.5
Adenine	1.2	1.0	—	1.4	1.1	—	1.8	2.35	1.5	0.4	0.7	0.93
8-hydroxy-7-methyl-guanine	Not determined	0.75	—	1.0	0.8	—	0.6	1.32	0.2	Not determined	Not determined	0.97
Guanine	0.4	<0.2	—	<0.2	<0.2	—	<0.2	<0.2	<0.2	<0.2	<0.2	0.2

Purine excretions are expressed as mg. excreted in 24 hours. Specimens stored were kept at -25°C . for periods specified in the Table. For experiments 2a, 2b and 3a the subjects had been receiving chlorpromazine in daily doses of 250-450 mg.

and seven months. Change even after seven months was not large, but probably implies a small loss in most constituents on storage (Table VIII).

(c) Appreciable differences were found in some purines when specimens were obtained from the same individuals at intervals of some months, and analysed without storage (Table VIII). Weissmann *et al.* (1957) also reported such differences.

OTHER DETERMINATIONS

The volume and pH of the urine were noted. Creatinine was determined in 0.5 ml. specimens by adding 20 ml. sat. aqueous picric acid, 1.5 ml. 10 per cent. w/v NaOH, allowing to stand for 15 minutes, and adding water to 100 ml. After 10 minutes optical density was read at 520 m μ . On keeping at 0° the urine specimens which had been collected over chloroform, their creatinine content was found to fall after some months, though creatinine standards similarly stored were stable. This occurred to similar degrees in acidified urines and in others left without adjustment of pH. A 24-hour specimen originally containing 1.62 g. creatinine lost 5 per cent. of its content in 47 days and 16 per cent. in 82 days.

The creatinine determinations were carried out and are recorded because it was considered desirable to include the estimation of a well-investigated urinary constituent in the present study. Urinary creatinine values can give an indication of gross deficiencies in the completeness of the collection of the day's urine output. Such incompleteness was not encountered in the present study, for the collections were carefully made. Creatinine excretion is reported in Tables V, VI, IX and X in terms of body weight, and it will be noted that the values imply a fairly wide range of "normal" variation in creatinine excretion: in males, from 21 to 32, mean 24.9 ± 4.0 (5) mg./kg., and in females, from 12 to 25, mean 18.8 ± 4.2 (7) mg./kg. The value of 20 mg./kg. described by some writers as normal is recognized as susceptible to large variation (Folin, 1905; Hunter, 1928; Beard, 1943; Vestergaard and Leverett, 1958).

RESULTS

1. *Comparison of Schizophrenic and Control Subjects*

The purine excretion figures for the male and female groups are shown in Tables IX and X.

When the results for hypoxanthine are studied it is noted that in 6 out of the 10 pairs the patient's excretion of hypoxanthine exceeded that of the control. Application of student's *t* test to the data indicated that the difference fell well short of significance. This appraisal was not altered when body weight is taken into account (Fig. 3). Similarly when figures for xanthine are considered it is found that in 7 out of the 10 pairs the patients' excretion was higher than that of the control, but again the difference fails to approach significance. When the male and female groups are considered singly with respect to the substances the significances of the differences are not increased. When the output of the other purines is reviewed the schizophrenics and controls seem to be a homogeneous group.

Since there appeared to be no striking group differences between the patients and the controls, individual variations from the group means were examined in terms of particular purines and specific clinical features—severity of illness, duration of illness, and form and course of these illnesses. No relationship was apparent. It is, for example, evident from Tables IX and X

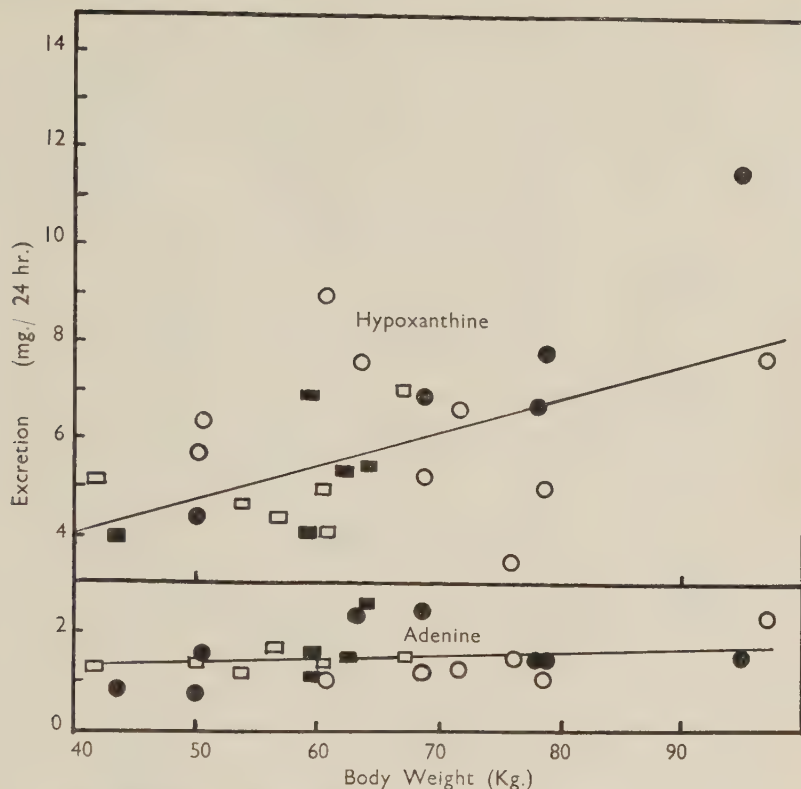


FIG. 3.—Daily excretion of hypoxanthine and adenine by 14 men and 14 women. Half of each sex were schizophrenic and half were normal subjects who were approximately matched in age and weight. The lines show the calculated regression coefficients.

that hypoxanthine excretion was particularly high in patients 1 and 3. References to these patients' case histories, however, failed to indicate that these two men differed clinically from the remainder of the group or that they displayed particular clinical features in common. Again, xanthine output was low in patients 2 and 3; 1-methyl and 7-methylguanine output was high in patients 3 and 8. Hypoxanthine and 7-methylguanine excretion was raised in patient 1 but there was no discernible connection between these variations and the characteristics of the illnesses from which the patients suffered. Furthermore, it will be seen from Tables IX and X that the control subjects showed deviations of similar frequency and magnitude to those of the patients. On this evidence it may be suggested that marked deviations in output of the purines were without clinical significance. Purine excretion was also unrelated to the particular treatment of drugs which had been administered to the patients in periods prior to those in which urine specimens were collected for the present studies.

2. Variation with Body Weight

Although variation in the excretion of endogenous purines in the present experiments was considerably less than in those from dietary sources (see below), there were sufficient differences within the groups of 28 males and females

TABLE IX
Purine Excretion in Male Subjects

Pair	Person	Age (years)	Weight (kg.)	Urinary Volume (ml./24 hours)	Creatinine (mg./kg.)	Hypo- xanthine	Xan- thine	1-methyl and 7-methyl- guanine	Purine Excretion (mg./24 hours)					
									8- hydroxy- 7-methyl- guanine	Adenine	Para- xanthine	1- methyl- xanthine	7- methyl- xanthine	
1	..	30	95	1,540	11.5	11.6	4.2	2.5	1.55	1.45	—	6.6	23.4	17.2
1	C	37	97	3,380	13.2	7.7	4.9	2.8	2.34	1.47	—	13.6	19.0	20.3
2	..	23	78	1,080	17.5	6.7	1.6	4.6	1.46	—	0.32	3.7	5.2	17.3
2	C	32	76	2,600	20.6	3.5	2.9	2.1	1.5	0.91	—	9.4	10.2	13.9
3	..	35	78.5	2,250	13.9	7.8	2.0	8.9	1.4	1.0	—	5.6	17.0	8.9
3	C	29	78.4	2,290	23.2	5.0	1.1	2.4	1.2	—	<0.2	3.0	3.0	2.4
4	..	22	50	1,167	21	4.4	3.3	2.8	0.75	0.64	<0.2	—	—	—
4	C	22	50	1,630	31.6	5.7	2.3	3.5	1.4	0.2	<0.2	—	—	—
5	..	17	50.5	8.5	23.5	6.4	3.9	1.6	1.6	1.0	<0.2	—	—	—
5	C	18	60.5	1,406	20	9.0	1.8	1.1	1.1	0.44	0.2	—	—	—

* Schizophrenic. C, control subject from whom samples were obtained at the same time, and analysed together with the corresponding patient.
C was chosen as similar as possible to the patient in age and weight.
—; Not determined.

TABLE X
Purine Excretion in Female Subjects

Pair	Person	Age (years)	Weight (kg.)	Urinary Volume (ml./24 hours)	Creatinine (mg./kg.)	Purine Excretion (mg./24 hours)									
						Hypo- xanthine	Xan- thine	1-methyl and 7-methyl- guanine	8- hydroxy- 7-methyl- guanine	Guanine	Para- xanthine	1- methyl- xanthine	7- methyl- xanthine		
6	..	23	64	1,590	19.7	5.4	6.7	7.1	2.6	2.0	0.4	26.6	40	4.3	
6	C	25	53.5	1,340	19.7	4.6	4.9	3.0	1.2	1.1	0.4	12.4	12.5	1.6	
7	..	30	43.5	1,040	18	4.0	3.9	3.5	0.95	0.97	<0.2	—	—	—	
7	C	29	60.3	1,070	15	4.1	2.95	4.0	1.34	<0.2	<0.2	—	—	—	
8	..	25	59.4	2,000	18.5	6.9	5.6	2.94	1.6	—	0.4	—	—	—	
8	C	27	41.5	1,700	21.6	5.1	5.0	2.5	1.3	—	0.4	—	—	—	
9	..	48	59.5	1,342	23	4.0	4.0	3.2	1.1	1.2	0.4	—	—	—	
9	C	48	67.0	1,670	15	7.0	8.4	6.15	1.5	2.0	<0.2	—	—	—	
10	..	28	62.0	1,160	12	5.4	5.0	5.4	1.5	0.43	<0.2	—	—	—	
10	C	28	56.5	1,080	20	4.4	3.4	5.0	1.64	0.3	<0.2	—	—	—	

* Schizophrenic. C, control subject from whom samples were obtained at the same time and analysed together with the corresponding patient.
C was chosen as similar as possible to the patient, in age and weight
—: Not determined.

(Tables IV, V, VI, IX and X) to merit examining whether the variation was correlated with body weight.

The rate of *hypoxanthine* excretion is plotted against body weight in Figure 3 and shows considerable scatter, but a tendency to increase with increasing body weight. Two men over 90 kg. in weight gave the highest excretion rates, whilst the females who tended to be of lower weight than the males, are grouped almost exclusively in the lower half of the curve (Fig. 3). The calculated regression coefficient was 0.07, corresponding to a correlation coefficient of 0.28 and a P value of 0.05 to 0.1.

Plotted in a similar manner, the daily *adenine* excretion proved to be almost independent of body weight. Values for 1- and 7-methylguanines and for *xanthine* were too variable for a definite conclusion to be drawn. *Guanine* excretion was too small for comparable appraisal.

3. Age and Sex

Comparison of the male subjects (patients and healthy controls), with the corresponding female series (Tables IX and X) indicated differences between the sexes in the excretion of certain purines. Most noticeable in this respect was the smaller excretion of hypoxanthine in women, although since their weight was lower than the weight of the men, a certain difference would be expected for this reason alone. Also, the earlier analyses included more men and seasonal factors could be involved. In order to examine more closely any dependence of excretion on sex, specimens from normal men and women who were matched in age and weight were collected and analysed together (Table IX). In these experiments also, output of most purines was greater in the men. This applied to hypoxanthine.

The majority of the individuals examined were under 30 years of age. The highest value for hypoxanthine in men are in those aged 30 or over (Table IX) although this was not the case in the women. Excretion of other purines did not appear to be closely correlated with age.

4. Dietary and Endogenous Purines

Much of the purine excretion from subjects drinking ordinary quantities of tea, coffee or cocoa consists of caffeine, theophylline, theobromine or their metabolites, that is, mainly methylated xanthine and uric acid derivatives (Christman, 1952; Sollmann, 1957). The present methods are fully adequate for the determination of these metabolites as well as the endogenous purines, and such determinations were made in a proportion of the subjects under investigation, because abnormal metabolism of a dietary purine would be relevant to the present study. Values are included in Tables IX and X. These show 1-methylxanthine to be excreted at rates ranging from 3 to 40 mg./day, 7-methylxanthine at 2–20 mg./day and paraxanthine at 3 to 14 mg./day. These widely-spaced values were found to be approximately correlated with wide differences which were noted in the intake of tea or coffee. Differences were not observed between normal subjects and patients, but as can be judged by the values quoted, large differences only would have been significant. The large range of values observed in the excretion of the dietary purines, contrasts with the much narrower range observed in adenine, xanthine, hypoxanthine, guanine and methylated guanines (Tables IX and X), which were the main subject of the present study.

DISCUSSION

Excretion in Normal Subjects

The methods for determining urinary purines devised by Weissmann *et al.* (1957) were found readily adaptable to the present study. Before appraising findings in mentally-ill subjects the following characteristics of the methods employed and of purine excretion in normal subjects, are to be noted.

Recovery experiments: dietary factors. The division of the purines estimated into two groups, one greatly dependent on the intake of beverages containing caffeine and related compounds, and the other independent of these, is supported. Data on the first category of compounds, quoted in Tables IX and X, lie within a rather wide range of values quoted by Weissmann *et al.* (1957) and earlier observers. The other category of urinary purines, which may be termed endogenous, has been the subject of careful recovery experiments (Tables IV to VII), for recovery experiments of this type do not appear to have been carried out previously. Our results are actually similar to those of the recovery experiments made by Weissmann *et al.* (1957) from an "artificial urine" prepared from a limited number of pure substances contained in urine. Such a mixture must omit many more compounds than it includes, and thus recovery from urine itself is considered important. Recovery in the present experiments was excellent or fairly good in the cases of hypoxanthine, adenine and guanine, but of some 64 per cent. in the case of xanthine. The range of values found for excretion of "endogenous" purines from the present subjects usually overlapped with those reported by Weissmann *et al.* (1957); individual compounds are considered below. It is however a notable conclusion of the present study that excretion can depend markedly on bodily characteristics of the people examined, especially on their body weight and sex. That these characteristics have not been recorded in sufficient detail in earlier studies, limits the comparisons which can be made between the present and earlier findings, but the following conclusions can be drawn.

Hypoxanthine. The mean daily excretion of hypoxanthine by the present subjects of some 6 mg./day is appreciably lower than that found by Weissmann *et al.* (1957), of 9.7 (range: 7.4–12.5) mg./day. Recovery of added hypoxanthine in the present experiments was excellent, and the divergence from Weissmann's results must be attributed to a real difference between the two groups of subjects. Here the results of Figure 3 are important, for they show a marked dependence of hypoxanthine excretion on body weight, such that within the range of body weight examined a 2-fold difference can be attributed to this factor.

The other important characteristic now found to condition hypoxanthine is sex, as is apparent from Tables IX, X, XI and from Figure 3. The mean values from the investigation as a whole were: from men 6.78 and from women 5.09 mg./hour, that from the men being 1.33 times that from the women. This is similar to the well-established dependence of creatinine excretion on sex (Beard, 1943; Hunter, 1928). Indeed the mean value for creatinine excretion, per kg. body weight per day in the men now studied, was found to be 1.33 times that of the women.

Xanthine. The mean value for the daily excretion of xanthine by the present subjects, of 3.83 mg., is also about two-thirds of that found by Weissmann *et al.* (1957), which was 6.1 mg.; recovery of xanthine in the two studies was about the same. Figure 4 shows that we find large individual variations in xanthine among different people, though Table VIII indicates relatively constant values

TABLE XI

Purine Excreted in Male and Female Subjects Examined Together

Experiment number	1		2		3	
Subject (sex)	J.S. (male)	H.R. (female)	R.R. (male)	E.P. (female)	R.H.C. (male)	— (female)
Age (years)	27	29	40	43	30	35
Weight (kg.)	71.5	60.5	63.5	67	68.5	66.5
Urinary volume (ml.) ..	3,040	890	1,200	1,420	1,743	1,083
Daily creatinine (mg./kg.) ..	21	17	21	18.3	28	25
Purines (mg./24 hours):						
Hypoxanthine	6.6	4.6	7.6	3.55	5.2	5.2
Xanthine	3.7	3.25	3.7	3.3	4.0	2.0
7-methylguanine	3.2	1.7	3.92	4.0	4.5	2.2
Adenine	1.23	1.01	2.45	1.25	1.5	1.2
8-hydroxy-7-methylguanine	0.2	0.12	0.3	0.73	1.72	0.7
Guanine	<0.1	<0.1	0.1	0.2	<0.1	<0.1

Each experiment with a pair of subjects (one male, one female matched approximately in age and weight) was carried out as described in Table V.

in a given person examined on different occasions. No correlation with body weight is apparent in all or in any one of the four categories of subjects illustrated in Figure 4. There is also no consistent difference between the sexes in xanthine excretion; although Tables IX and X would suggest greater excretion in women than in men, this trend is not borne out by the determinations of Table XI which were made on samples which were collected and analysed together. Here the men give the higher xanthine values. We place greater reliance on this latter result as the experiment was designed with sex as the main variable; the collections and chemical analyses of Table IX were in most cases carried out a few months before those of Table X.

Other compounds. Excretion of adenine by the present people, of 1.45 mg./day, is close to the value of 1.4 mg. found by Weissmann *et al.* (1957). It has not been found dependent on the weight or age of the subjects, but all the values for men in Table XI are greater than those for women. Guanine is excreted in markedly lower quantities, of some 0.2 mg./day, which the present methods did not evaluate. Nevertheless, the recovery experiments of Table IV show that any appreciable increase in guanine excretion would have been detected; none was observed.

Excretion in Schizophrenia

The point at which direct comparison can be made between the present results and those of Kishimoto (1958) is in xanthine excretion. Here the Japanese workers reported excretion from schizophrenic subjects to be 2.7 times that from normal subjects, the difference being statistically significant. This contrasts with the findings of the present study, summarized in Figure 4. From this Figure it is clear that xanthine excretion is very variable in both normal and schizophrenic subjects, the extreme values among the 28 people quoted differing by a factor of 5. This readily gives scope for the finding of groups from whom excretion differs 2.7-fold. Indeed a 2-fold difference in excretion was found between two of the subgroups examined in the present study. Excretion by the female schizophrenic patients differed by this factor from that of the male control subjects. However, the male control subjects showed only a quite small difference from the male schizophrenics with whom they were matched in age, weight and in the collection and analysis of the specimens. Also, values from

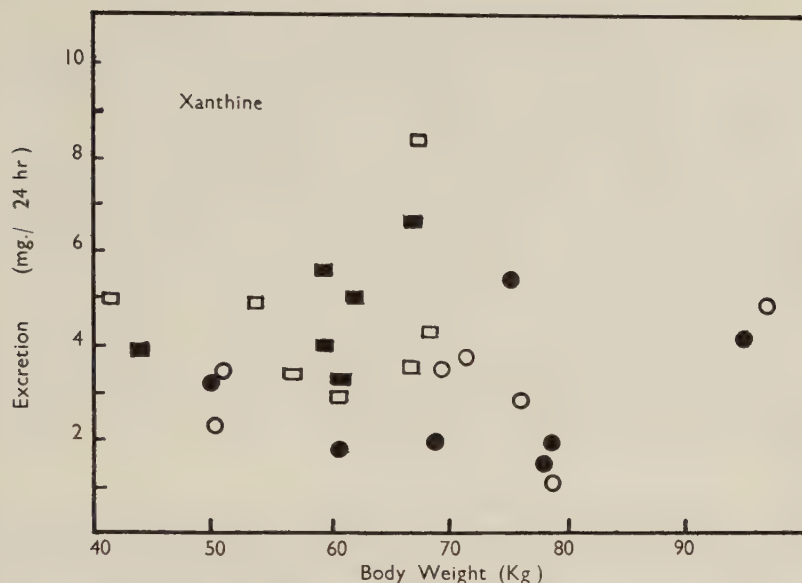


FIG. 4.—Daily excretion of xanthine by the subjects described in Figure 3; symbols and other details as described in Figure 3.

the female schizophrenics were very close to the female control subjects with whom they were similarly matched.

The latter observation gives a practical demonstration of the virtues of the experimental design chosen in the present study. To see whether illness conditions excretion, it is clearly most valuable to match a particular patient with an individually chosen control subject and to collect and analyse the paired specimens together. This chosen design minimized the likelihood of finding artefactual differences between schizophrenic and control subjects. Understandably, it did not control so effectively the other factors examined. In particular, the temporal sequence in the study, which was such that most of the women were examined before the men, made necessary the subsidiary study of Table XI. This probably would not have been necessary had the main investigation alternated the examination of matched pairs of women with matched pairs of men. Comparable details of experimental design are not reported by Kishimoto (1958) and no opinion is therefore expressed as to why his results differ from our own, except that the experimental sequence and physical differences between subjects can greatly influence findings.

The present study of urinary purines in schizophrenia goes much beyond that of Kishimoto (1958) in that the five or six other compounds of Table XI were examined with the same experimental precautions as have been described in relation to xanthine. In none was significant difference found to be associated with the illness. Observations on other compounds, and further studies of the effects of treatment, will be reported subsequently.

SUMMARY

1. Methods for repetitive determination of six endogenous purines in urine have been evaluated by recovery studies. They have been applied to the measurement of hypoxanthine, xanthine, 1- and 7-methylguanines, adenine, 8-hydroxy-7-methylxanthine and guanine in one or more 24-hour specimens from 28 subjects.

2. Ten of these subjects were suffering from severe and clearly defined schizophrenic illnesses. They were matched one by one with 10 normal persons in age, weight and sex, and the collection and analysis of specimens from each patient carried out together with that from the corresponding normal person. Urinary creatinine was also measured.

3. No differences were found between schizophrenic and normal groups in excretion of the compounds named. This applied to xanthine, the excretion of which has been reported to be abnormal in schizophrenia. Those who were highest or lowest in excretion of a particular compound were not of unusual mental status.

4. Physical characteristics were however found to condition purine excretion. This was marked in the case of hypoxanthine, excretion of which increased with increase in body weight. Excretion of hypoxanthine was also greater in men than it was in women of similar weight. This variation with sex was found in most of the compounds studied.

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A REVIEW OF STRESS REACTIVITY RESEARCH IN RELATION TO PSYCHOPATHOLOGY AND PSYCHOPATHIC BEHAVIOUR DISORDERS

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INTRODUCTION

IN a series of papers concerned with the problems of repeated psychopathic and delinquent behaviour, use has been made of a loose theory which interprets the social behaviour or habit as being a particular learned response to stress, anxiety or emotional disturbance, or to stressor stimuli not necessarily activating physiological stress (190-200). This theoretical position was adopted on account of its relative simplicity, its similarity to many clinical theories, and its ease of access for laboratory and operational studies. In a mainly adult hospital setting, the area chosen for research has been the differentiation of stable and unstable patients, the determination of methods which allow for accurate prognosis of future stability or instability and the form which future instability might take. The objective also contains the assumption that an explanation of instability should be in a form which permits therapeutic endeavour or at least indicates some basic principles for therapy to adopt, and utilizes variables which change as the patient changes.

Experimentally based theories which use concepts of stress reactivity are being applied to an increasingly wide range of psychiatric and psychosomatic disorders (e.g. Davis, 40; Wolff, 207). It seems likely that operational studies of many different psychiatric problems will use the derived theoretical concepts and techniques in the future (Bindra, 19) although at present some topics remain relatively unexplored (*vide* Chalke, 32, on depression). The purpose of this paper is (a) to analyse particularly relevant developments in the general field of stress reactivity, (b) to summarize the practical conclusions and principles which are generally accepted, and (c) to offer a theoretical synthesis of the different views put forward by psychological research workers. In doing this we shall pay particular attention to the theoretical concepts associated with the notions of Stressor and Motivation on the one hand, and Responses and Individual Differences on the other hand.

BEHAVIOUR THEORY

The first requirement is to derive working principles for anxiety research which in turn permit definition and the clarification of ideas. The complexity of this problem is well demonstrated, for example, by the well-known Applezweig Bibliography (4) which lists 2,611 references to recent anxiety and stress research

* Medical Research Council Scholar.

and the present writers could add many more to this particular list which excludes much European and Russian work. There is some truth in the comment that anxiety research doesn't add up very fast but it certainly does multiply (Blake and Mouton, 22). Much of this intensive research by psychologists and physiologists remains unknown to psychiatry (Altschule, 2). Psychiatric applications of Behaviour Theory in Britain have been discussed by Davis (39).

At this stage, for the present purposes, anxiety and stress are used as synonymous terms describing a state of physiological or experiential disturbance brought about by the disruption of the state of the organism. This type of definition can be expanded in neurophysiological terms (e.g. Hebb, 90; Schaffer, 172; Seward, 176), and although we have introduced a differentiation between physiological and experiential disturbance, it is appreciated that an experiential factor of any kind, unaccompanied by physiological activity of *some sort* would be contrary to contemporary views. The differentiation is between (a) gross physiological activity, mainly visceral, and associated with autonomic functioning which in turn is associated with higher nervous activity taking the form of an "experience" or percept, and (b) the "experience" alone with its cerebral correlate, on the other hand.

Stimulus conditions which generally produce a state of stress are termed stressors, a term which will be analysed in some detail later. (The term "pressor" has sometimes been used apparently synonymously with stressor, e.g. Innes, *et al* (99)). Reaction to a stressor, at the behavioural or autonomic level, is given the term response, and is extended to include an organized pattern or activity sequence.

As a starting point we can adopt the position of Miller (151), in assuming that fear is an innate response to pain, and may also be learned. Fear is learnable because it can be learned as a response to previously neutral cues; fear is a drive because it can motivate the learning and performance of responses in the same way as hunger, etc. Working from a Hullian position (Hull, 97, 98), Miller puts forward two hypotheses, (a) that learned drives such as fear, obey the same laws as do overt responses, and (b) they have the same drive and cue properties as strong external stimuli. Fear, therefore, is a stimulus-producing response ($R \rightsquigarrow S$), i.e. a response to environmental stimuli which in turn functions as a stimulus to which overt responses are conditioned. In simple form the schema is $S \rightarrow R \rightsquigarrow S \rightarrow R$. The intervening variable $R \rightsquigarrow S$ can then be given a physiological connotation.

A closely allied interpretation is to regard fear as a not directly observable acquired anticipatory response to pain, having at least two of the functional properties of primary drives in the formal Hullian interpretation of the roles of drive and drive reduction (Montague, 152). The Hullian requirements of the drive property of anxiety or fear are that its reduction should be reinforcing or should strengthen responses immediately preceding its reduction, and should intensify any response tendencies that are present during its period of evocation.

There are, however, two types of learning situation involving pain, which contain important differences to which we shall refer frequently. The first situation is well described as Traumatic Escape Learning, and involves the continuation of trauma until the organism applies the response which terminates the trauma. In this situation, stress, and presumably fear, is necessarily activated, by definition, and learning is straightforward drive reduction. However, the second type of situation is Traumatic Avoidance Learning, in which case the conditioned stimulus precedes the unconditioned stimulus by a period of time sufficiently long for the organism to apply a response *which will prevent the*

unconditioned stimulus from occurring. During the latency period between CS and R an animal will show, at least in the early stages, the physiological concomitants of fear, so that one can assume that the learning link between fear and the overt response is one of drive reduction, and in accordance with Hullian principles. (There are difficulties in this explanation to which we shall return.) However, drive reduction cannot satisfactorily explain the learning of fear, the link between the CS and the arousal of physiological fear activity. This can only be explained by contiguity conditioning, so that at present we can reasonably adopt the position of Skinner (179) and later Mowrer (154) and Eysenck (52, 53), who suggest that there are two different mechanisms of learning, i.e. contiguity conditioning for the smooth muscles, glands and emotions (the link between the CS and the $R \rightsquigarrow S$ of fear), and drive reduction for the skeletal muscles (the link between the $R \rightsquigarrow S$ of fear and the overt behaviour).

Hence, with fear defined as the stimulus producing response to pain, anxiety can be defined as generalized fear, diffuse fear, or the conditioned fear reaction. It may be that this definition is partly traditional but it certainly draws some support from experiments with animals subjected to massive pain trauma who later show a symptomatology analogous to psychiatric "anxiety states". Possibly more relevant are the studies which show reduced pain and fatigue thresholds for psychiatric patients, particularly those suffering from anxiety states (Hardy, Wolff and Goodell, 87; Hemphill, Hall and Crookes, 93; Hall and Stride, 85; Stengel *et al.*, 183, 184).

ASSESSING ANXIETY IN HUMAN SUBJECTS

Although the definition of anxiety as generalized fear closely related to pain is fairly reasonable, the first objection is that this definition is far too narrow. Apart from the possibility of innate fear, there are many experimental situations which produce obviously learned disturbances akin to anxiety but could not be deduced from the definition we have adopted. These include frustration tasks and conflict situations, deprivation of stimulation and methods which are derived from *ad hoc* assessment of individual situations. In this last group would be experiments designed to re-activate supposed fear conditions by the recounting of emotionally loaded stories to neurotics (Jacobsen *et al.*, 101, 102), by confronting convicted murderers with relevant material (Luria, 124) and presenting startling life situation pictures to parachutists in training (Basowitz *et al.*, 9).

Even more removed from traditional theory are other stressor conditions which use mental arithmetic, tachistoscopic stimuli and perceptual devices such as the Rorschach, which are all supposed to arouse stress, but which are devoid of coherent theoretical rationale.

Apart from the multiplicity of stressor conditions used in research, there is the additional complexity of the response. In essence this should be at either the physiological or overt level, although the methods are numerous. The former include such diverse measures as skin and body temperature change, the galvanic skin reflex, blood cell counts (especially eosinophils), saliva output, pH value, K/Na balance, and tyramine-like content (Schenker and Schenker, 173), hippuric acid secretion, 17-ketosteroid day to night excretion ratios, blood pressures (for practical purposes, usually systolic), heart rate, respiration change, adrenaline excretion, the alpha rhythm, muscle potentials, blood oxygen saturations (Lovett Doust and Schneider, 123), etc. At the overt behavioural level the response index can be pain perception, reaction or resistance, designed

choice reactivity ostensibly measuring aggression, regression or withdrawal, verbal behaviour, visual perception, learning rates and performance. In some areas particular progress has been made in the recording and analysis of processes which have hitherto been the subject of qualitative assessment only (e.g. Goldman-Eisler, 74, 75, on analysis of the speech process under stress).

To complicate the psychology of stress even further, bodily diseases, medication, climatic conditions, exercise, diurnal variability and oestral factors, produce physiological changes of the sort which might be used to indicate a person's psychological stress reactivity (Wright, 212). Change in the eosinophil count, for example, is a frequently used index of stress reactivity, but for Antarctic explorers it has been shown that this index is affected by widely dissimilar tasks (Simpson, 177, 178). Finally, of course, although the psychology of stress and anxiety is far from complete, the physiology of many aspects of the subject is equally obscure.

In certain studies questionnaire methods are used to determine levels of anxiety, but results of these are notoriously difficult to interpret. Apart from the obvious statistical shortcomings of these techniques with the arbitrary summation of many different verbalized stressor responses, questionnaires are more likely to record "attitudes" and "opinions" rather than statements of fact. For these reasons we shall not review questionnaire research in any detail.

We propose that research studies should be classified according to the level of response, i.e. overt or physiological, and the nature of the stressor, applied. If the nature of the stressor is derived from the Miller definition of anxiety as a learned response to pain, or is closely associated with this definition and therefore restricted to particular stimulation, the stressor is described as Specific. In this way direct stimulation of a pain point would be a Specific Stressor, but we would also include techniques such as the cold pressor test, eye puff and startle stimuli. If the nature of the stressor could not be derived from the Miller definition, and therefore involves conceptual activity on the part of the subject, the stressor is described as Generalized. In practice, Generalized Stressors would appear to be divisible into at least two groups involving interference with different levels of drive. In animal studies Generalized Stressors usually involve interference with primary drive activity such as food seeking, or escape (e.g. Masserman, 147; Maier, 129; Knopfmacher, 109, 110; Marx, 146) but human studies usually apply secondary social drives with obvious indications of ego involvement and personal achievement interest (e.g. Marquart, 145; Jones, 105; Kay, 108; Miller and Swanson, 150).

This classification is similar in some respects to the biological "Hierarchy of Stressors" proposed by Fischer and Agnew, (57, 58), to explain the limited responsiveness of schizophrenics to certain stressors, and the relative infrequency of psychosomatic disorders in people under severe life-stress conditions. Fischer and Agnew classified stressors according to their capacity to threaten the various levels of organization of the organism, so that a "life stressor of primary importance" ranks higher than an "alarming" stressor and elicits different adaptive responses.

It will be noticed that we use the term "specific stressor" in a different sense from that originally used by Malmö and his associates (133-141). For Malmö a "specific stressor" is a stimulus with a particular stress connotation for a specified individual. The implications of stress reactivity research are that the abnormal arousal levels of anxiety for maladjusted people cannot be explained entirely in terms of specified or unique situational reactions, so that the notion of a "specific stressor" in the Malmö sense has no great practical

application. Clarke (34), for example, found that certain words produced motor responses indicative of disturbance in both neurotic and normal soldiers. The difference between the groups was one of degree, not kind. Furthermore, we find that there is difficulty in restricting the use of the Malmo term, and a tendency to extend the notion of stressor specificity in this sense from being descriptive of an individual to being descriptive of groups of people with some common experience, e.g. parachutists in training, for whom certain situations are necessarily stimulating. In addition the widely accepted notion of Response Specificity which refers to the restriction of effector functioning logically requires that the notion of Stimulus Specificity should refer to the restriction of affector functioning, which is the sense in which we prefer to use the term. A stressor which is unique to an individual or to a defined group of subjects can be termed a Special Stressor.

Occasionally, stressors are classified as being either physical (or physiological), or psychological (e.g. Heilbrun, 92; Bovard, 23) with the difference being due to the argument that psychological stressors "do not directly affect body cells, and hence must be mediated by the central nervous system" (Bovard, 23). With human subjects, of course, it is difficult to conceive an experimental situation in which C.N.S. mediated conceptual activity is not somehow involved. When a study requires the application of a succession of stressors, the time interval between stressors may be of fundamental importance. It is possible that there is an optimal time interval which would overcome what has appeared from G.S.R. work as the "halo" effect when stimuli are in close temporal proximity (Boyd and Valentine, 25), and the "incubation" effect when experimental extinction is delayed (Bindra and Cameron, 20).

STRESSORS AND MOTIVATION

One of the most significant methodological developments of recent years has been the acceptance of the principle that in stress reactivity study the researcher must have control over the stimulus conditions. In general, knowledge and theory concerned with the stressor lags behind those concerned with the response, but nevertheless there would be agreement with Malmo (133) that some form of stimulation is definitely superior to merely taking records under resting conditions. The only measure which would appear to discriminate between patients and controls under resting conditions is frontalis-muscle potentials (Malmo and Smith, 140), and one is forced to the conclusion that so called "resting conditions" do not provide basal scores and are probably stress conditions to an unknown and varying extent. This is well illustrated in a report (Glickstein, 71) of a factorial analysis of systolic and diastolic blood pressures, and heart rate, where the testing period extended over several hours, and could partly explain the absence of statistically significant differences between the blood pressures of anxiety cases and others, which is so frequently noted (Rudolph 168).

In experimental work, specific stressor stimuli are usually direct pain stimulation, faradic shock or some form of mild startle stimulus such as a puff of air to the eye, touching the eye with cotton wool or a momentary bright flash of light (Bassett and Ross Ashby, 10). The majority of studies which apply pain stimuli do so at the cutaneous level and there is a tendency at present to regard a person's pain threshold in a unitary fashion. Psychologically it may well be necessary to differentiate pain thresholds according to the nature of the stimuli necessary to elicit pain. Stimuli such as cutting, pricking, etc., which elicit

somatic pain capable of definite localization, do not elicit visceral pain which follows contraction, stretching, oxygen deficiency, etc., and which is incapable of definite localization and is often referred (Rothlin and Berde, 1967). Not only is pain a non-unitary concept, but there are differences in performance on a reasoning task according to whether a specific stressor is applied for poor attainment with or without prior verbal warning (threat), which again demonstrates the complex nature of even the most simplified stressors (Heilbrun, 92). It appears that "threat" does not interfere with performance level with a dynamometer type of task, although it reduces the subject's estimate of his attainment (Dearnaley, 41).

Cutaneous pain responses have been studied in some detail with the radiant heat dolorimeter (Hardy, Wolff and Goodell, 87), but it is essential to define closely the response being assessed, i.e. perception or verbal report, or reaction, which is usually withdrawal, or resistance. These overt responses correlate highly with one another although the perception or verbal report of pain index is greatly affected by a subject's attitudinal or motivational state (Hall, 82, 83; Hall and Stride, 85; Tong, 195). This attitudinal factor, which may be the stress index used in one particular research, could on other occasions distort the results of what was intended to be an "objective" study. Kamin (106), for example, has reported the existence of a variate of "apparatus stress" which correlates with the mechanical aptitude score of normals and their familiarity with electrical apparatus.

The results of Specific Stressor studies suggest that these tests can be useful indicators of general anxiety, stress reactivity, or emotional disturbance. Earlier or more marked reactivity to pain, or lessened pain tolerance, etc., has been widely reported for psychiatric patients in whom anxiety or emotional disturbance is a prominent, or could be an expected symptom (Hemphill *et al.*, 93; Hall, 82, 83; Hall and Stride, 85; Malmö *et al.*, 131, 136, 137, 138, 139; Tong, 191, 195). However, there is not always a high agreement between a pain index and psychiatric diagnosis. In discussing this, Stengel *et al.* (183) suggest that a pain index is more indicative of a factor of "Overt Reactivity", inherent in which is the patient's general reactivity to all types of stimuli. Later we shall discuss the possibility that there are two types of anxiety, pain-fear anxiety, and ego involvement anxiety, and it may well be that the divergence between laboratory induction and psychiatric assessment is due to this difference. Stengel draws attention to the high degree of inter-correlation for the scores obtained by different pain techniques, a finding in line with that previously reported for normals (Clark and Bindra, 33). Kamin, *et al.* (107) found that the Taylor Anxiety Scale and pain tolerance are two distinct unrelated variables, and suggest that the questionnaire measures general upset or arousal under stress, whilst the pain score indicates avoidance tendency.

Similar conclusions could be drawn from the work of Piercy *et al.* (159) who used faradic shock stimuli and psychogalvanic indices of pain expectancy derived from studies of prefrontal leucotomy and pain expectancy (Elithorn *et al.*, 47). Patients rated for their level of clinical anxiety did not differ correspondingly in their pain tolerance levels, but did differ by a tendency to form anticipatory sets which were accompanied by a relatively greater degree of autonomic disturbance. That the psychological, attitudinal factor of cutaneous pain perception is highly associated with related autonomic functioning can also be concluded from studies of pain perception and skin temperature (Hall, 83; Tong, 195). From the practical point of view overt responses to specific stressors such as pain do not seem to be greatly affected by age or intelligence,

although both should rightly be controlled in comparative studies (Hall and Stride, 85; Tong, 191, 195; Stengel *et al.*, 184).

Although work with specific stressors seems to hold promise it is advisable to be cautious when data are extended to *explain* psychopathological phenomena and to bear in mind the artificial nature of the laboratory tests. In a discussion of pain research with patients who are prone to self-inflicted injury, Stengel has pointed out that self stimulation can be different in its conceptual context from stimulation by another person or by a machine (Stengel *et al.*, 184, and personal communication).

In recent years much attention has been paid to the use of conditioning devices as indices of anxiety or stress reactivity although not all conditioning procedures concern stress reactivity (e.g. Bindra *et al.*, 21, on salivary conditioning). Specific stressor stimuli are the most common with the response being either autonomic change or a closely defined overt response such as eye-blink, finger withdrawal or muscle contraction, although novel techniques are available (e.g. Tizard, 189). This particular work is discussed below with particular reference to the problems of individual differences.

Laboratory situations which apply Generalized Stressor conditions have been concerned mainly with motivational issues when the research has been clinically oriented, even if not especially directed towards the solution of clinical problems. On the other hand, human engineering studies which are frequently concerned with the breakdown in performance of people under stimulus stress conditions, have made considerable progress in the analysis of the complex stimulus conditions which lead to inefficient or maladjusted responses (e.g. Conrad, 36). Clinical studies have much to gain by paying closer attention to the work in this field (Bartlett, 8). Noise, for example, which greatly affects performance in normals (Broadbent, 26), has been relatively unexamined as a stressor in laboratory work with psychiatric patients and military studies frequently provide suggestive data about stress reactivity (e.g. Renbourn *et al.*, 162, 163).

For diagnostic and prognostic purposes, Generalized Stressor techniques have two important limitations. In the first place the patient must be able to understand the task with which he is confronted, and in the second place he must be sufficiently well motivated to make a genuine attempt towards a solution. When normals are used as research subjects they are usually selected for their ability to undertake the required task, but a similar task applied to psychiatric patients may either be incomprehensible in an immediate sense, or in a wider conceptual sense. Simply reducing the complexity of the stressor may still leave the conceptual aspect unaffected. Air-force pilots faced with experimental flying stress situations in a laboratory cockpit (Davis, 38), would have a different concept of the task from a control group of non-pilots even though the latter perform the required movements. With a very simplified stressor such as mirror drawing (Malmo and Davis, 135), we find that although this is well within the skill limits of people between 50 and 80 I.Q., the task involves less for them than it does for highly literate people for whom a pencil has long been an extended digit in so far as control is concerned. Similarly we find that a stressor such as having to name quickly the colours in which a series of colour names are written (Stroop, 186) is greatly affected not only by ability to read but by the familiarity of the subject with written material and the importance of a reading skill to him. (We have observed that this technique produces an interesting "blocking" phenomenon of short duration for doctors and psychologists during which period there *seems* to be no ideation activity and

which is paralleled by autonomic changes, but this is less frequent in nurses and virtually absent in literate mental defectives although reading speeds for colour words are roughly the same for each group.)

The addition of incentives to generalized stressor experiments is unlikely to affect the main motivational factor. If, as seems probable, generalized stressor techniques only activate stress in subjects for whom the situation involves personal achievement drives and ego defences, cigarette and money incentives will not achieve a similar state if used to arouse interest in others. This statement may require qualification when advantage is taken of electromyographic techniques (Benson and Dearnaley, 15, 16; Malmö, 133) which provide objective measures of the degree of arousal occasioned by incentives.

The ego involvement factor may well operate in more tests than is appreciated and we have pointed out elsewhere that indices such as emotional reaction and anxiety on the Rorschach test correlate not with physiological reaction to Specific Stressors but with reactions to Generalized Stressors in which ego defences and achievement drives are involved (Tong and Murphy, 199).

Cox (37), in his discussion of learning experiments with questionnaire selected anxious and non-anxious subjects, explains the frequent divergence in results as being partly due to a failure to recognize that even "high anxiety" subjects do not form a homogeneous group in respect of their differential reactions to social and non-social stimulation—factors usually present in a laboratory test situation.

Lazarus and associated workers have emphasized the motivational factor, insisting that psychological stress involves the thwarting of a motive state, and that reactivity to experimental stressors is also influenced by cognitive control and the limitations of the experimental situation (Lazarus *et al.*, 122; Vogel *et al.*, 203, 204). An important differentiation is made between "induced" and "intrinsic" motivation, with the latter being described as the relatively enduring motivational characteristic of an individual. In a general review of research in this field (Lazarus and Baker, 121), a common criticism is made of many stress reactivity studies. In the majority of experiments, stress has been defined implicitly or explicitly, in operational terms (i.e. in terms of a stimulus situation which is considered stressful by the experimenter) and a plea is also made for more appreciation of the role of individual differences.

In spite of these problems, and the practical limitations of Generalized Stressors, these techniques are extremely valuable in the examination of theoretical problems concerning the application of stress reactivity theory to clinical or real life problems. It seems likely that the most valuable function of Generalized Stressors is to simulate aspects of real life situations or skills. Masserman's work with cats (147) helps in the understanding of conflict situations and the research associated with Maier's frustration theory (129; Maier and Ellen 130), has stimulated much important work. From the results of animal studies Maier suggests that behaviour under frustration is non-goal directed, non-motivated and different in kind from other forms of (adaptive) behaviour which is directed to reduce a drive, but this view has been challenged by others who suggest the Maier experimental situation and results can be explained by anxiety reduction theory (Farber, 55; Mowrer, 154; Knopfmacher, 109, 110). Nevertheless, Maier's classification of frustration instigated behaviour into aggression, regression, resignation and fixation is important. In the fixation studies, Maier found that under frustration conditions the majority of animals develop position stereotypes in their jumping responses. Of the animals who develop stereotypes a good proportion cannot learn a

subsequent soluble task and continue to show the response which was developed under frustration. This is then termed a position fixation, and is regarded by Maier as not being anxiety reduction motivated and not directed towards the solution of a problem, but simply the end product of frustration. Maier has offered interesting speculations concerning human behaviour disorders, and in particular recidivism is seen as fixated behaviour in view of the inefficiency of punishment as a means of re-education and repression (p. 88); if stereotypy is shown in the overt behaviour, then fixation is apparent (p. 190).

Human studies of frustration behaviour suggest that Maier's theory oversimplifies the situation but nevertheless cannot be wholly rejected. Marquart (145) reported a bimodal post-frustration learning curve, as would be predicted by Maier, and demonstrated the significant importance of the motivational factor entailed in the size of the faradic shock which was administered for "wrong" responses. Jones (105) demonstrated stereotypy in humans, but found that the extent of stereotypy varied according to the motivational level or degree of achievement drive which he manipulated in his subjects. Kay (108) found non-adaptive behaviour under experimental frustration to be more common for neurotic children than delinquents or controls. Russell and Steinberg (169) found that inhalation of stress reducing nitrous oxide during frustration resulted in better post-frustration learning, and suggested that post-frustration learning impairment is due to the anxiety aroused by frustration, contrary to Maier's original opinion. Tong (195) found that roughly 60 per cent. of psychopathic and delinquent subjects showed a skin temperature fall (a stress response) during frustration, but those with this physiological anxiety response had lower regression scores. In addition, when high degree position stereotypy occurred this was almost invariably associated with a temperature fall, so that regression and position stereotypy appeared to be frustration phenomena of different psychological orders. Regression was regarded as an *avoidance-learned* habit, which tends to prevent anxiety from occurring, and stereotypy as a response to activated stress. Stereotypy, temperature fall and post-frustration learning impairment were features more pronounced for normals than patients.

RESPONSES AND INDIVIDUAL DIFFERENCES

Verbal and performance learning tasks (as opposed to conditioning situations) have been common tools in stress research for some years and there has been some examination of the effects of stress on various perceptual processes (Postman and Bruner, 160; Granger, 77; Callaway and Thompson, 28; Kohn, 111; Korchin, 112; Weckowicz, 206). With learning tasks anxiety is either assumed to be aroused by the task, or the drive is some form of achievement motive, or else anxiety is assumed to be manipulated by rewarding correct responses and punishing incorrect responses by verbal comments such as "right" and "wrong". For the vast majority of these studies it is difficult to form any conclusion as to the value of the data owing to the lack of evidence that the particular experimental situation did in fact arouse anxiety. Many studies classify people into anxious and non-anxious subjects by means of a questionnaire and then *assume* that a particular experimental situation will arouse anxiety in one group and not in another. This is a waste of research time when physiological techniques for measuring arousal are readily available. Nevertheless, it seems likely that anxiety as a drive facilitates learning in these situations (e.g. Gordon and Berlyne, 76; Montague, 152), although when pathological groups are considered, results are not always consistent, and it is

very difficult to determine whether these tasks for adult human subjects involve new learning or the application of established habits. Foulds (59, 60), for example, applied a maze learning task and found the main differentiation to be between normals, psychopaths and hysterics on the one hand and anxiety states, reactive depressions and obsessionals on the other. However, Hall and Crookes (84) applied a word pair learning task and a switch task to mixed neurotics and found that in almost all respects the anxiety cases came closest to the normals on these tasks. In this report it is noticed that when compared with hysterics, anxiety state subjects do relatively well at word-pair learning, but relatively poorly at trial and error learning. The latter test could probably be better construed as a frustration situation for the anxiety group in which "hypotheses" are continually being discredited, possibly analogous to interference with established habits. This would account for the apparent breakdown in performance by the anxiety cases.

It now seems essential for learning experiments to be designed so that it is clear whether anxiety functions as a drive or as a disrupter. If the stressor is aimed to disrupt established responses by requiring new responses or modification then results are usually more clear cut. In so far as motor activity is concerned, Davis (38) has described the pathological reactions of air force pilots applying a skill under stress. These experiments are proving to be of considerable interest to clinical and social studies. Davis' initial description of the over-reactivity reaction in presumably anxious (or ego involved) inefficient pilots on the one hand, and the inertia reaction of other inefficient pilots is explained in terms of anticipatory tension and its inhibition, respectively. Venables (201) examined this motor response variate in relation to hysterics and anxiety states finding that an increase in task difficulty produced inertia in the former and over-activity in the latter, with a tendency towards the reverse relationship when the task became easier. More important, however, Venables (202) found that the increase in tenseness was accompanied by an increase in skin conductance, but whereas increased activity by "normals" produced a decrease in conductivity, this did not appear to be so for neurotics who could not, apparently, "work off" the disturbance. (This is similar to the observations that contemporaneous overt motor activity reduces sudomotor activity in response to mild stressors, Freeman and Pathman (63), and Haggard and Freeman (81). Anthony (3) has subsequently examined the relationship of this psychomotor variate with military delinquency, finding that delinquents differed significantly from non-delinquents both in manner of reduction and increase in task difficulty. The increase in task difficulty used in these studies consisted of an increase in both the speed of stimuli presentation and the complexity of the stimuli, together. In an attempt to verify and utilize this approach to stress reactivity, we have found that psychopathic and delinquent subjects in the lower intelligence ranges (60-80 I.Q.) cannot satisfactorily handle the dual load of speed increase and complexity, and when these are considered separately it is the speed load, not the complexity load, which introduces stress and the motor behaviour variations (Tong *et al.*, 200).

In the same way that one can discern a certain amount of rationalization and systematization in the psychological work on stress reactivity, there has been similar progress in biological studies. More important, however, work is no longer being undertaken in isolation. It seems likely that biological measures are more closely related to real life criteria than psychological measures, but psychological theory and experimental design are essential before the biological data make sense. Biologically based studies (e.g. Basowitz *et al.*, 9) have been

forced to recognize the two types of stressor conditions which we have previously described as the pain-fear situation, and the ego-involvement situation, and which resemble Kamin's factors of avoidance tendency and general upset (Kamin *et al.*, 107). Basowitz describes two types of anxiety, shame anxiety or fear of failure, and harm anxiety, which correlate with one another but to the experimenter there may be only one unitary state of emotional distress. The indications are that these two stressor conditions differ in their effects on the adequacy of functioning at all biological levels and, of considerable practical importance, the harm anxiety indices differentiated successful from unsuccessful parachutists (*op. cit.*, p. 273), with the biochemical variables being the most reliable measures (p. 279). Similar conclusions were reached in our analysis of stressors and responses in relation to relapse for delinquent and psychopathic subjects (Tong, 195). Basowitz used hippuric acid secretion measures and the eosinophil count, and in this case found the eosinophil measure to be more efficient. The eosinophil count is one of the simpler biological measures and has, of course, been used often (e.g. Dreyfuss and Feldman, 43; Sands and Bartler, 171; Murphy *et al.*, 155; Simpson, 177, 178), owing to its relative ease of access for quantification and statistics, although apart from an association with adrenal functioning (Wright, 212) relatively little seems to be known of the function of the cells or the mechanism which brings about their disappearance in stress conditions.

Autonomic responses have probably received more attention than other physiological measures, with the result that many older theories are now known to be over-simplifications. Cannon's interpretations of the functioning of the A.N.S. (Cannon, 30, 31) have been challenged particularly by a series of studies by Lacey and his associates. They point out that whilst the A.N.S. does function as a whole in response to stress, in the sense that all innervated structures seem to be activated, usually in the direction of apparent sympathetic predominance, the A.N.S. does not function as a whole in the sense that all innervated structures exhibit equal increments or decrements of function (Lacey and Lacey *et al.*, 113-119). Lacey works from the notion of "symptom specificity" formulated by Malmö (e.g. Malmö, 132) which states that in psychiatric patients with a somatic complaint the particular physiological mechanism of that complaint is specifically susceptible to activation by stressful experience. The principle of symptom specificity is extended to the principle of "relative response specificity" which is: "For a given set of autonomic functions subjects tend to respond with an idiosyncratic pattern of autonomic activation in which maximal activation is shown by the same physiological function, whatever the stress." And furthermore "the entire pattern or hierarchy of response is reproducible over different stressor episodes, and that continuous quantitative variation among subjects exists in the degree to which they exhibit stereotypy (reproducibility) of their pattern of response" (Lacey and Lacey, 117). The evidence in favour of these principles is very strong, and obviously complicates the problem of autonomic measurement in psychology (i.e. a single or double channel record is probably insufficient), and adds to the long-appreciated mathematical difficulty of how to evaluate a response, the magnitude of which is related to pre-stimulation level. Long appreciated with regard to skin resistance, at least, with the result that many varied, but all unsatisfactory, transformations and measures have been tried, e.g. per cent. resistance changes, log conductance changes, the square root of conductance, etc. (Haggard, 79, 80; Lacey and Siegel, 120; Paintal, 158; Elliott and Singer, 48; Bassett and Ashby, 10; Venables, 202; Tong, 191; Woodworth and Schlosberg, 210.)

Mathematical solutions to both difficulties exist but before considering these it is worth while bearing in mind that there are two possibilities which may, in practice, offer solutions which are simpler than multi-channel recording and complex mathematical transformation. The first is that although there tends to be little inter-response agreement when the response *per se* is measured, there might be more agreement if *conditioned* responses are measured. (Martin, 144, reports a very low correlation coefficient between a conditioning score for the G.S.R., and basal skin resistance, but a low coefficient between basal score and late acquisitiveness, although the technique applied resembles avoidance conditioning rather than contiguity conditioning.) The second possibility is that nosological types or special groups of subjects may show greater inter-response agreement, or differences at all response levels than a random group of normals.

The mathematical solution for the evaluation of autonomic responsiveness offered by Lacey (113) rests on an explanation that the negative relationship of the magnitude of stress induced A.N.S. change to pre-stimulation level is due to homeostatic restraint of response and not simply due to response limitation. Consequently the common practice of removing the regression of algebraic response on initial, or pre-stimulation level, is regarded as erroneous, and as an alternative Lacey applies a score based only upon the regression of stress level on initial level. The results are termed autonomic lability scores. (This is the deviation, in sigma units, of attained stress level from expected stress level, with the latter being the average stress level estimated by regression lines attained by subjects having the same pre-stimulation level as the subject under consideration; Lacey and Lacey, 118.)

Some autonomic responses, particularly the galvanic skin response, lend themselves readily to conditioning procedures so that attempts have been made to evaluate the strength of anxiety as a drive by using some index based upon the conditionability of the response to mildly noxious stimuli. The index is usually the number of conditioned responses established in a set period, or the rate at which C.R.s are established, or extinguished, or variations on these scores. Similar methods of scoring are applied to other conditioned responses such as the eyeblink, finger withdrawal, anticipatory responses of muscle tension, etc. At present it seems that these conditioning studies hold out considerable promise for the future, and much attention has been paid to inter-individual variations. With fairly efficient techniques data seem to correlate highly with real life criteria (Tong, 195, 196; Franks, 62; Lykken, 125). and individual differences are readily demonstrable. However, we have found that although test-retest reliability is very high for 90 per cent. of delinquent and psychopathic subjects, about 10 per cent. fluctuate from one end of the conditionability scale to the other over intervals of several months, and furthermore although there is a high correlation coefficient between the results for two slightly different conditioning devices using similar stimuli and responses, this is by no means as high as theory demands (Murphy, I. C., to be published). For reasons we mentioned earlier we feel that data concerning the correlation between conditioning scores and "anxiety" questionnaires serve only to confuse (Taylor, 188; Spence and Taylor, 182; Sampson and Bindra, 170).

Explanations of individual differences in stress reactivity are all very similar, and the concepts of varying strengths of excitatory potential or inhibitory potential or both are frequently applied. Stengel's description of Overt Reactivity as the degree of psychomotor reactivity of a patient at any given time (Stengel *et al.*, 183) as the factor which determines his response to a

painful or threatening stimulus, seems to bear a similarity to Eysenck's postulate of variation in excitatory potential (Eysenck, 51). The concept of variation in inhibition, or reactive inhibition to explain differences in stress reactivity has been suggested by Hall (85, 86), in respect of pain and reaction time, Malmo (133) for various anxiety reactions, and in relation to excitation, also by Eysenck. It should be noted that in general Malmo suggests that psychoneurotics *as a whole* are less affected by reactive inhibition (Malmo and Wallerstein, 141).

Eysenck's formulations (49-54), not only attempt to rationalize the problem of individual differences, but also draw together the two main problems of pathological stress reactivity, i.e. under-reactivity and over-reactivity. The extent to which Eysenck's learning theory postulates would be acceptable to Hull or to Pavlov is probably not important. Pavlov apparently changed his mind about regarding hysteria as a pathologically intensified phenomenon of inhibition (Ivanov-Smolensky, 100) and Hull fluctuated over the use of a concept of inhibition, but certainly conceived the possibility of individual differences in the magnitude of his constants in his Postulate 17 (Hilgard, 95). The main problem of the explanation of individual differences in terms of excitation and inhibition is to relate this to the overt behaviour patterns which constitute psychiatric illnesses or behaviour disorders. Whether the pathological condition is constitutional or not, or whether it comes about by over-stimulation of stress mechanisms, does not explain how or in what way the obviously learned behaviour phenomena come about.

An explanation of delinquency and psychopathy offered by Franks (61, 62), and Eysenck (54), is that the relatively low excitatory balance of the psychopath, which is demonstrable by his low conditionability (an accepted laboratory fact) means that he cannot "form those conditioned reflexes which we call learning the rules of society". This sort of explanation will not bear clinical analysis, of course. The description fits the imbecile, not the psychopath, and completely misses the point that the psychopath knows the rules of society but fails to observe a select few. Similar difficulties apply to explanations of hysterical disorders and compulsions, etc., and obviously what is needed is an explanation of the particular symptoms of these patients.

THEORETICAL SUGGESTIONS

The synthesis we propose uses the notion of individual variations in the inhibitory factor, not for the learning of overt behaviour directly, but for the conditioning of the intervening stimulus producing response of fear, which we suggest would lead to corresponding variations in the establishment of avoidance-learned habits. A very efficient inhibitory factor, or rapid establishment of reactive inhibition for physiological fear would lead to relatively rapid traumatic avoidance learning, whereas a poor inhibitory factor for physiological fear would bring about a disrupting effect in performance showing itself in relatively poor learning, but marked agitation and continued physiological activity. These extremes would show themselves as the psychiatric syndromes of relatively intractable habits of some cases (traumatic avoidance-learned habits), and the agitated behaviours of other cases.

This proposal or hypothesis requires a close analysis of traumatic avoidance learning. In doing this we draw freely from the work and suggestions put forward by Solomon and Wynne (181), who start from an acceptance of anxiety as a stimulus producing response, and a duality position of classical contiguity

conditioning for the link between the overt stimulus and physiological (stimulus producing) response ($S \rightarrow R \rightsquigarrow S$), and instrumental drive reduction conditioning for the link between the physiological (response produced) stimulus and the overt response ($R \rightsquigarrow S \rightarrow R$). Soloman and Wynne do not consider the effect of variations in the strength of the inhibitory factor for the $R \rightsquigarrow S$ of fear as we have suggested. They do, however, draw attention to four phenomena of traumatic avoidance learning for dogs which cannot be explained by simple Pavlovian conditioning laws, particularly as applied to extinction. These four phenomena appear to be analogous to aspects of certain psychiatric disorders. They are:

1. Once established the traumatic avoidance-learned habit can be elicited repeatedly without any signs of extinction, and without reinforcement. (In Pavlovian law repetition of a CR in absence of reinforcement brings about extinction.)
2. Overt signs of anxiety disappear in the animals who also become more stereotyped in their responses, and the latency between the conditioned stimulus and response becomes shortened.
3. Preventing an animal from making the avoidance response brings about intense fear reactions.
4. A long latency between conditioned stimulus and response results in anxiety reactions.

Psychiatric analogies of these, particularly in the field of conduct disorders, could be the poor response to therapy of some cases; the possibility that psychiatric therapy reinforces unwanted habits in some cases perhaps by generating anxiety, as does punishment (*vide* Radzinowicz, 161, for the effectiveness of different methods of treating sex offenders); the absence of manifest anxiety in some disorders, yet the occasional, unpredictable, emotional upsets (e.g. in the primary psychopath and hysteric).

To explain items 2, 3 and 4, Soloman and Wynne point out that once a traumatic avoidance habit is established, the animal usually responds so quickly to the conditioned stimulus that there is no time for physiological anxiety to be aroused, yet, of course, anxiety *is* aroused if the time interval is sufficiently long. "In one sense, the amplitude of the anxiety reaction is being *conserved* as a relatively intact potentiality, a latent functional entity." This is described as the Principle of Anxiety Conservation, but it is appreciated that even with this principle, extinction (item 1, above), should eventually take place. To overcome this difficulty, Soloman and Wynne suggest a Principle of Partial Irreversibility of Classical Conditioning . . . "a traumatic or very intense pain-fear reaction taking place in the presence of some conditioned stimulus pattern will result in a *permanent* increase in the probability of occurrence of an anxiety reaction in the presence of that conditioned stimulus pattern (whenever it occurs)". The suggestion is that the anxiety reaction will decrease during extinction trials but will never be completely eliminated, remaining permanently at some fixed level above zero. (This idea would be in accordance with Hull's concept of sH_R which is preserved as a fixed quantity. Extinction for Hull is deduced by subtraction of sI_R and I_R from sH_R for computing the effective reaction potential, sE_R).

This principle would find support from a wide variety of different sources. In psychiatry Cameron (29) has said "Once a person has been rendered anxious over a long period he tends to be over-reactive to situations likely to produce anxiety"; Selye's description of the three stages of the general adaptation

syndrome (Selye, 175) implies permanent change particularly in relation to the output of A.C.T.H. and adrenaline. Gellhorn (69) readily accepts the notion of permanently lower thresholds for ANS discharge. Malmo (133) suggests the possibility that weakened inhibition for anxiety may occur in a manner similar to the way in which the after-discharge of the cerebral cortex can be abolished in the reticular formation of the thalamus and the brain stem and quotes work by Jasper (103) and Moruzzi and Magoun (153). (Malmo accepts the notion of inhibition as a process independent of excitation possibly transmitted chemically as indicated by Eccles (46).)

We have proposed that pathologically high inhibition for anxiety would lead to more rapidly established avoidance habits highly resistant to extinction. As far as we are aware there is no direct evidence from animal studies indicative either of these variations in the strength of the inhibitory factor or their effect on learning. However, it seems reasonable to make such inferences from the data discussed by Solomon and Wynne, and various incidental observations. Beach (11, 12), for example, described the varying effect of faradic shock on the sexual behaviour of different animals of the same species, and Solomon and Brush (180) emphasize that failures of animals to learn to avoid are not rare but these are less apt to be reported in scientific journals than the successes.

Having traced a rather devious route in presenting these speculations, it may be of value to summarize the main points we have raised. These are:

1. From a duality theory of learning one can present a structural definition of anxiety linked to pain or trauma. Research studies applying stressors based upon this sort of definition appear to provide data which correlate highly with real life criteria, particularly when biological responses are measured, although the accurate assessment of autonomic responsiveness is likely to be more complex than was once thought.

2. There are other situations which arouse physiological anxiety in some people and which could not be deduced from the pain-fear definition. These involve conceptual activity on the part of the subject, and motives concerned with ego defences and achievement drives. Data from this sort of research may serve to give insight into certain situations but would probably correlate poorly with real life situations in which pain-fear, not failure-fear, was the operative mechanism. Some generalized stressor situations may be analogous to traumatic avoidance situations in that the "punishment" is not a UCS, but a CS long established to the basic pain-fear link.

3. Individual differences in stress reactivity are usually explained in terms of variation in the strength of reactive inhibition for *overt* responses. This introduces difficulty in translating formal explanation into clinical terms, particularly when it is necessary to explain why some habits and not others come to be learned.

4. We have suggested that variation in the strength of reactive inhibition applies to the establishment of the physiological response of fear. In addition, pathologically high inhibition leads to easily formed and well fixed avoidance-learned habits (analogous to certain psychiatric disorders associated with extraversion), and pathologically weakened inhibition leads to agitated anxious overt behaviour (introvert psychiatric disorders).

5. This suggestion enables one to explain different disorders as traumatic avoidance-learned habits (when stress need not necessarily be activated) or traumatic escape learned habits or agitation (when stress is activated by definition).

STRESS REACTIVITY APPLIED TO RECIDIVISM AND PSYCHOPATHY

The foregoing review has been drawn from a wide variety of sources and concerns not only work with mentally fit people but studies with many different psychopathological conditions. The writers have been mainly concerned with operational research with delinquent and psychopathic patients, which has required a re-phrasing of the problem in scientific terms. Apart from any intrinsic interest that this approach to delinquency may bear, it illustrates the application of stress reactivity work in psychiatry.

The inter-related basic problems of psychopathy and recidivism are how to predict, accurately, the future conduct of an adult with a long history of offences, and how to change his conduct. Failure to recognize that these are the special problems for psychology and psychiatry leads to criticism that experts merely remove one set of moral judgments and provide another (Wootton, 211). Undue concern with problems of non-scientific concepts such as "responsibility" has been criticized by Macdonald (126), who would be supported by Bowman's comments (24), indicating that psychiatry has fared no better than a penal system with the psychopath problem in the U.S.A. and the conclusion that psychiatry has been oversold. Similar conclusions could be drawn from a comparison of recidivism rates given by Radzinowicz (161) for sexual offenders dealt with in this country by referral either to psychiatrists or the penal system.

There have, of course, been several social psychiatric and sociological attempts to come to grips with prediction (Glueck and Glueck, 73; Mannheim and Wilkins, 142, and references), but although these reports indicate that it is at least possible to predict behaviour, the systems fall short of the main requirements. These requirements of a suitable predictive method have been given elsewhere (194), and are:

1. The method must be highly accurate.
2. It should indicate degrees of stability and instability, and the form that instability might take.
3. It must be applicable to the individual case. This comment implies caution in the interpretation of group derived data, and rational flexibility in the methods of assessment.
4. The information should indicate therapeutic requirements.

In spite of the obvious shortcomings of behaviour theory, there is at present no other theory which opens up a methodological approach capable of offering a predictive system able to satisfy these criteria. It also seems necessary, at present, to recognize and utilize the role that anxiety, or its apparent lack, performs in the structure of delinquent and psychopathic personalities, although it is possible that sex responsiveness is a separate factor to consider for some sex offenders (Tong, 197). Virtually all clinical writers have commented upon the anxiety factor in some way. Freudian literature associates to a large extent the delinquent and the neurotic, but at the same time writers have attempted to search for differences between the two disorders (e.g. Freud, 65; Aichorn, 1; Healy, 88; Healy and Bronner, 89; Friedlander, 66; Fenichel, 56). Throughout these clinical accounts occur descriptions of two extreme pathological types although these types may be covered by one heading. Fenichel (p. 324), differentiates between the neurotic with possible sexual compulsions, and the impulsive psychopath by suggesting that the former is disturbed by his disorder (i.e. stress-reactive) and the latter not (i.e. not stress-reactive). Freud (64)

describes pedophilia as the perversion of weak and impotent persons (anxiety interference) but Hollitscher (96) refers to the absence of affect in homosexual attachments. Other writers imply abnormality in emotional reaction or specifically, anxiety (e.g. Burt, 27; Stott, 185; Glueck, 72), whilst I.Q. and age factors have been found to be relatively unimportant except possibly as general factors (Woodward, 209; Marcus, 143; East, 44, 45; Benson, 13, 14; Ogden, 156). The significance of the emotional factor can also be inferred biologically from the observations by Sturup (187), concerning castration and Garst and Stobin (68) on variations in day to night excretion ratios for 17-ketosteroid excretion for different types of sex offenders.

McCord and McCord (148) in their review draw attention to the general agreement that certain psychopaths are characterized by the absence of anxiety. Within the Eysenckian framework, Franks (62) has suggested that recidivism is associated with either poor conditionability (extraversion), or high conditionability (introversion), and Lykken (125) has indicated differences between the conditioning scores of primary and neurotic sociopaths. Attempts to verify the Eysenck hypothesis by the use of questionnaire methods have been unsuccessful presumably due to the unreliability of questionnaire methods in this field, at least (Robin, 165; Bartholemew, 7). By using relatively objective methods based upon stress reactivity work, the bipolar nature of psychopathic instabilities can be demonstrated (191, 195), particularly with closely defined conditioning techniques. Equally important, it is possible to indicate the differences between certain forms of behaviour.

At this stage one can put forward certain tentative propositions which we feel must be borne in mind in subsequent work. They are:

1. The basis of continual psychopathic instability, is faulty anxiety or fear responsiveness, which consists either of over- or under-responsiveness (physiologically) to stressors.
2. Research based upon the interpretation of anxiety as stress responsiveness, indicates that techniques which assess the physiological response to specific stressors carry a far higher relationship to social criteria than other methods (which may only serve to confuse).
3. Instability due to stress unreactivity (high inhibition) would show itself as:
 - (a) impulsive behaviour undeterred by clearly apparent sanctions (e.g. aggressive rape), or
 - (b) well-established stereotyped traumatic avoidance patterns in reaction to relatively minor stimuli (e.g. running away, larcenies, indecent exposures, and some aggressions).
4. Instability due to abnormally high stress reactivity (low inhibition), would show itself as agitated panic behaviour, or chronic anxiety behaviour (e.g. suicidal gestures, aggression, indecent assault).

These propositions indicate the need for differential research in respect of the different forms of overt conduct disorder. Differences have been indicated in previous reports (191, 195), but considerably more remains to be done. Rich (164) has examined different types of stealing; Davis (39) has referred to the similarity of certain incomplete sexual behaviour as being similar to that of experimentally neurotic animals, and there is indication of biochemical stress reactivity differences for different types of sex offender (Garst and Stobin, 68). Nevertheless, it seems hopeful that an operational approach of this nature

using the concepts and methods derived from stress reactivity research can achieve important practical results.

SUPPLEMENTARY CONSIDERATIONS

Although much stress reactivity work is not widely known this paper has not been aimed to provide a comprehensive review. We have been particularly selective but nevertheless most areas of the topic, theoretical, practical and applied have been mentioned, and this final section refers briefly to four additional facets which are likely to have some impact during the next few years.

Neurological interest in the conditioned reflex has been present from the early propositions of Pavlov, but it required the speculations of Hebb (90) to bring the great bulk of psychological thinking into line with the neurological developments. (On the other hand it is also possible to reduce the Hebbian neurological principles into behaviour theory terms, e.g. Berlyne, 17.) There are many problems in behaviour analysis probably better contained by physiological theory and research (Hebb, 91), and similarly some problems are better contained by psychological theory. However, stress reactivity is probably not only the most urgent problem requiring the contributions of both disciplines, already the case, but also in need of neurological rationale. It is in this aspect that there are likely to be significant changes in emphasis. Interest is shifting from cortical explanations of conditioning and in particular the inhibitory process, to the brain stem reticular activating system (Jasper, 103; Magoun, 127, 128; Malmo, 134). Jasper, in particular, emphasizes that although it appears possible that the mechanism of arousal (and hence motivation), lies in the reticular system, this is at present far from proven, but the experimental results do at least permit working hypotheses even though tenuous theories are still required to explain psychological phenomena. Nevertheless, it is hopeful that this work and its association with "activation" explanations of "emotion" will do much to rationalize the situation (Cofer, 35; Rosvold, 166).

Of possibly more immediate practical interest are the research findings which suggest that in different states of emotion different types of adrenomedullary secretion take place, noradrenaline for rage and adrenaline for fear (Gellhorn, 70). Arnold (5) summarized a good deal of the evidence of parasympathetic ascendancy in assertive or angry responses, but this was in turn questioned by Ax (6). However, Ax's work did reveal a tendency for the pulse and respiratory rates to be raised in fear and lowered in anger. Psychologically more significant is the work by Wolff and Wolff (208) which pointed out that in response to a threatening situation the stomach showed either under- or over-activity. Different individuals tended to show one or the other predominantly, but the most important factor affecting the reaction was the individual's conception of the situation, i.e. whether he felt defeated or not. More recent work is that of Funkenstein and his associates (67) and it is possible that the disagreements which exist in the research on this topic are largely due to the different uses given to the terms "anxiety" and "fear" by different authors (Gellhorn, 70). In general it now seems likely that applied laboratory work must accept a schema, much as follows:

	<i>Anger</i>	<i>Fear</i>
Hypothalamic excitation ..	Relatively high	Relatively low
Autonomic activity ..	Parasympathetic ascendancy	Sympathetic ascendancy

	<i>Anger</i>	<i>Fear</i>
Adrenals	Noradrenaline	Adrenaline
Laboratory measures:		
Pulse rate	Lowered	Raised
Respiration rate	Lowered	Raised
Blood pressures	Mild increases in systolic and diastolic	Marked increases in systolic

Throughout this review we have considered mainly the work concerned with reactivity to what may be termed "positive" stressors, i.e. situations in which stimulation of some sort is applied by the researcher. Post-war studies concerned with stimuli or sensory deprivation and isolation suggest that these "negative" stressors are of considerable psychopathological significance (Bexton *et al.*, 18; Heron *et al.*, 94; Doane *et al.*, 42; Scott *et al.*, 174; Mendelson, 149). Unfortunately it appears that fundamental work in this field, probably of very high quality, will be late in being reported for the benefit of mental health research owing to its importance in space travel research (Wase and Christensen, 205) and it would be valueless at this stage to speculate in what direction the results will affect future work. At the very least we can expect to find that certain forms of isolation, particularly social isolation (which may include loneliness in a crowd), are stressors with particular action on C.N.S. mediated activity. Apart from "negative" stressors, the extent and intensity of positive stressors is an aspect still to be examined in detail. It is clear from the work of Oswald, for example (157), that severe stressors administered over a long period produce effects both of different and higher orders than those we have discussed in this paper.

Finally, it is of fundamental importance for research in this field to be able to take advantage of the advances in instrumentation. Oscillographic recording apparatus and systolic pressure recorders are now readily available, and pick-up devices are no longer cumbersome and alarming. In the near future progress in a wide range of pathological studies may be accelerated by the introduction of the military apparatus (e.g. Grieve, 78), which has been designed for transmitting physiological signals to the laboratory from subjects in real life stress situations.

SUMMARY

Recent literature dealing with experimental stress reactivity research is reviewed for the purpose of drawing attention to the developments in theory and technology. Reference is made to the two basic forms of stressor conditions, harm stressors and ego involvement stressors, and the importance of conceptual and motivational factors. Responses are measured at physiological or overt levels, and individual differences usually explained by means of variation in inhibition. Theoretical suggestions are put forward which enable different disorders to be classified as traumatic avoidance learned patterns or activated anxiety reactions, according to the strength of the inhibitory factor for stress. This approach is applied to a theoretical analysis of delinquency and psychopathy, in particular.

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FAMILIES OF DULL CHILDREN*

PART II.—IDENTIFYING FAMILY TYPES AND SUBCULTURES

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CULTURE in its anthropological sense has been described as “a configuration of learned behaviour and results of behaviour whose component elements are shared and transmitted by members of a particular society” (Linton, 1936); in other words, a way of life. It has long been understood that more than one type of culture may be found in any one society. All societies are stratified and in an industrial society people of different levels have different ways of life. These are subcultures.

Culture has been thought to have an important influence on intelligence and achievement at school (Sarason and Gladwin, 1958). We therefore wished to study the families of dull children in Lancashire according to their subcultures. In order to do this, it was necessary to be able to identify such groups. This paper sets out our attempt to do so.

METHOD

The study was based on the families of a group of young adults who had been ascertained as educationally subnormal at school in Lancashire County and Salford City. The sample comprised one-third of those born between 1933 and 1936, drawn at random for each administrative area. Because of their age, almost all came from completed families. The 106 subjects and their 102 families were visited. All families save one and all subjects save seven were interviewed, and available agency records were checked for information relating to all.

Families were then classified by two criteria: occupation of father of the subject (according to the Registrar General's Classification of Occupations) and educational achievement of the siblings of the subject.

* This study was inaugurated by Professor C. Fraser Brockington sponsored by the National Association of Mental Health, and aided by a grant from the Halley Stewart Trust to one of us (Z.A.S.). The Medical Officers of Health of Lancashire County Council (Dr. S. C. Gawne) and of Salford County Borough (Dr. J. L. Burn) made the survey possible by seconding field workers.

RESULTS

FAMILY TYPE (Table I)

TABLE I
Classification of 102 Families

Family Category	Occupation of Father	Social Class	Education of Siblings	No.	Group Totals
Aspirant ..	Small business	II	Grammar school	3	9
	Small business	II	None in grammar school	1	
	White collar	III	None in grammar school	2	
	Skilled manual	III	Grammar school	1	
	Unskilled manual	V	Grammar school	2	
Artisan ..	Skilled manual	III	Elementary or secondary modern school	12	12
Rough:					
Intact	{ Semi-skilled Unskilled	IV	Elementary or secondary modern schools	43	
Structure ..					
Dysmorphic	Mainly casual labourers			13	56
Dull:					
Intact	{ Semi-skilled Unskilled	IV	At least 1 sibling ascertained M.D. or ESN	17	
Structure ..					
Dysmorphic	Mainly casual labourers			8	25
Grand total				..	102

Within the 102 families of the 106 subjects the following groups were defined:

1. *Aspirant*

At least one child of these 9 families had achieved a grammar school education or the father was in a non-manual occupation in Social Class II or III.

2. *Artisan*

No child of these 12 families had achieved a grammar school education, but the fathers were skilled manual workers.

3. *Rough**

No child of these 56 families had achieved a grammar school education, and the father's occupation was semi-skilled or unskilled (Social Class IV or V).

4. *Dull*

In these 25 families a member other than the propositus had been ascertained educationally subnormal or mentally defective, i.e. more than one member of the sibship had been formally recognized as backward in school. Father's occupation was semi-skilled or unskilled (Social Class IV or V).

CHARACTERISTICS OF FAMILY TYPES

These family types differ from each other in such features as family structure, the use of social agencies, social mobility, migration, family size and church affiliation.

* This term is taken from Lupton and Mitchell (1953), who used it to describe families of similar type, as the families themselves did.

Family Structure

Twenty-one families, termed dysmorphic in another paper, were so damaged in structure that they failed to provide a set of enduring human relationships for their members; a home was not maintained and consequently the children were reared partly in institutions or foster homes. Thirteen dysmorphic families might be grouped as "rough" and eight as "dull". None were found among "artisan" or "aspirant" families.

In the results that follow dysmorphic families are set apart from those of intact structure, because the cultural environment of the children is formed as much by institutions as by families.

Use of Agencies (Table II)

TABLE II
Use of Agencies by Family Type
Numbers of Each Family Type Known to Selected Agencies

	Aspirant	Artisan	Rough	Dull	Dys- morphic	Total
Children's Department ..	0	0	0	5	17	22
National Society for Pre- vention of Cruelty to Children	0	1	2	6	10	19
School Attendance and Welfare Officer	0	1	6	5	7	19
Child Guidance Clinic ..	3	2	8	6	5	24
Mental Health Department ..	5	2	11	9	10	37
Total No. of Contacts ..	8	6	27	31	49	121
Total No. of families in sample	9	12	43	17	21	102

Community agencies may be of two main types. At one extreme are agencies which make use of legal sanctions or may easily invoke them such as the Children's Departments and the National Society for the Prevention of Cruelty to Children—they are in some senses disciplinary. At the other extreme are services which cannot invoke legal sanctions and which rely on voluntary relationships as the channel through which they provide their services. A good example of this type is the Child Guidance Clinic. Some services, such as Mental Health Departments in parts of Lancashire, may work in either way, depending on the individual case. "Dull" families were often known to both disciplinary and voluntary types of agencies, Aspirants had made use of the voluntary type of agency and Artisans and Roughts were little known either to the disciplinary or to the voluntary type of agency.

In their early twenties less than half of the Aspirants resided in a local authority area where at least one grandparent had been reared.

Half the Roughts still lived in an area where both a maternal and a paternal grandparent had been reared, and almost nine out of ten where at least one grandparent had been reared.

"Artisan" and "dull" families had migrated in much the same way as Roughts. Subjects from dysmorphic families were themselves very mobile and scattered over England.

Migration (Table III)

TABLE III						
Migration by Family Type						
Family Type	Total No.	A	B	C	D	
Aspirant	9	1	1	3	4	(44%)
Artisan	11	0	1	0	10	(91%)
Rough	42	2	2	2	36	(86%)
Dull	17	0	1	2	14	(82%)
Dysmorphic	20	3	1	3	13	(65%)
Total	99	6	6	10	77	(78%)

Key:
A. Subject now lives away from his birthplace.
B. Subject lives in the place of his birth, but his parents were not reared in that area.
C. At least one parent (but no grandparent) was reared where subject lives at present.
D. At least one grandparent was reared where subject lives at present.
(3 families, where the information was inadequate, are omitted from this analysis.)

Occupations of Fathers and Grandfathers (Table IV)

TABLE IV					
Occupations of Grandfathers in 102 Families by Family Type					
Grandfathers' Occupations					
Family Types	Social Class II or III Non-manual	Skilled Manual	Unskilled Manual	Not Known	Total
Aspirant ..	3	4	2	0	9
Artisan ..	1	3	8	0	12
Rough ..	3	9	40	4	56
Dull ..	2	5	13	5	25
Total ..	9	21	63	9	102

Only the grandfather highest in the social scale has been shown for each family.

The peak occupation of at least one grandfather was classified in 93 families and of both grandfathers in 61. Information was incomplete particularly from dysmorphic families and in cases of illegitimacy, and also because it was usually retrospective and given by the parents of our subjects, but it did enable us to examine social mobility between the generations.

In one family among Aspirants, both grandfathers and the father owned small businesses, while in two families one grandfather and the father were in non-manual occupations. Grandfathers of the remaining 6 families were manual workers.

One "artisan" family had a grandfather in non-manual work, 3 had at least one grandfather in skilled work, and the remaining 8 families had both grandfathers in unskilled work.

Among Roughs, there were three grandfathers in non-manual work, 9 families whose grandfathers were skilled men and 40 whose grandfathers were known to be unskilled.

Two "dull" families had grandfathers in non-manual work, 5 had grandfathers who were skilled workers and 13 had grandparents known to be unskilled.

Thus there was apparent evidence of a downward drift in six families. In one small "rough" family the paternal grandfather was a general dealer

(Social Class II) but this family still owned property and had some of the hall-marks of Aspirants. In another, the maternal grandfather was a stage-dancer, classified as Social Class IIIC. In these two cases, drift was more apparent than real and arises because no scale of social class can truly reflect social reality.

The paternal grandfather of one "artisan" family was a clerical worker and the father a ship's engineer who died before the birth of the subject. The father's family did not keep in touch with the children, who were drawn into the web of the mother's family. In one "dull" family the mother, with eleven children, described her father as a commercial traveller. Her husband, a skilled joiner, was working as a labourer at the time of the interview. In these two cases, the lowered social position of the families arose from difficult social circumstances.

Two cases illustrate mainly the effect of mental instability. A coal-dealer's daughter, of markedly dull demeanour and conversation, had had three illegitimate children (including the subject) by casual unions. Lastly, a housing inspector's daughter, of unstable character, married a weaver and then deserted him and her two young children.

Family Size

A regular gradient for family size increasing from "aspirant" through "rough" to "dull" is revealed by the family classification (Table V). The

TABLE V
Family Size and Family Type

Family Type					Number	Mean Size of Sibships
Aspirant	..	..	..	..	9	2.5
Artisan	..	..	..	..	12	4.5
Rough	..	..	..	..	43	5.1
Dull	..	..	..	..	17	7.1
Dysmorphic	..	..	..	..	21	4.6
Total	..	..	..	..	102	5.15 ± 2.9

The differences between "aspirant", "rough" and "dull" families are significant at the 1 per cent. level.

criterion for classification as "aspirant" or "dull" in our families depended partly on an exceptional education for siblings. In theory, therefore, the larger the family, the greater the chance of being classified as "aspirant" or "dull". In practice, grammar school entrants came from small families, so that this bias probably applies only in the case of "dull" families.

Social differences were found between Roughts categorized by family size. In large families more fathers were unskilled, more were Catholic than Protestant, and more use was made of agencies. Small "rough" families appear to have affinities with "artisan" rather than with large "rough" families. In the small "rough" families, too, occupations were more often semi-skilled than unskilled.

Church Affiliation

"Aspirant", "artisan", small "rough" and "dull" families were predominantly Church of England. Catholics were found particularly among large "rough" families, and none were found among Aspirants (Table VI). The number affiliated to other churches was small.

TABLE VI
Church Affiliation and Family Type

Family Type					Number	Church of England	Roman Catholic	Other
Aspirant	..	..	..	..	9	8	0	1
Artisan	..	..	..	..	12	8	2	2
Rough (sibship 5 and under)	..	..	..	..	26	21	2	3
Rough (sibship 6 and over)	..	..	..	..	17	9	7	1
Dull	..	..	..	..	17	13	3	1
Dysmorphic	..	..	..	..	21	11	9	1

Variations between denominational and lay schools in referring backward children for examination and "ascertainment" possibly account for some of these religious differences. Referrals are controlled by teachers and some denominational schools have low referral rates.

Acceptance of Examinations (Table VII)

TABLE VII
Selection of Cases for Examination by Family Type

					Inited		Not Invited	Total
					No. Patients Examined	No. Refusals		
Aspirant	..	..	..	..	7	0	2	9
Artisan	..	..	..	..	5	4	3	12
Rough (sibships 5 and under)	..	..	..	..	10	6	10	26
Rough (sibships 6 and over)	..	..	..	..	9	1	7	17
Dull	..	..	..	..	9	2	6	17
Dysmorphic	..	..	..	..	10	1	10	21
Total	..	..	..	..	50	14	38	102

Fourteen subjects refused the physical and psychological examination which was offered to 64 in all. The offer was accepted at the family interview but refused by the subject himself in all but one case, in which both family and subject refused. There were no refusals among the seven Aspirants invited, one among the 10 Roughs from large families, one among 11 from dysmorphic families and two from 11 "dull" families. But 4 out of 9 from "artisan" and 6 out of 16 from small "rough" families refused.

DISCUSSION

All the families in the sample formed part of a local culture. There were no members of highly mobile social groups with wide cultural affiliations such as, for instance, business executives or university lecturers.

The nine "aspirant" families may be taken to represent a social group distinct or emerging from the local culture. They have either maintained a position separate from manual workers, as they have potential upward social mobility through the education of their children. This mobility corresponds with their greater geographic mobility. Their aspirations towards middle-class values are presumably expressed in the educational attainments of family members, and on these assumptions the group will be described as belonging to an *aspirant subculture*.

They appear to make efficient use of agencies which volunteer services and they avoid contact with disciplinary agencies. Probably a similar attitude is reflected by their complete co-operation in the research. Families were small.

In contrast the 56 "rough" families are socially and geographically immobile in three generations, and they appear to form part of a stable cultural group in Lancashire urban areas. During half a century of social upheaval with two world wars, a major depression and severe unemployment, these families had hardly migrated. There is no upward gradient of skill or education in these families, and they gave no signs of upward social aspirations. This is a subculture distinct from the middle-class culture of these areas as represented by the local burgesses, for example owners of businesses, and still more distinct from the national middle-class culture of mobile professional groups (Watson, 1957). On these assumptions, "rough" families will be described as belonging to a *demotic subculture*.

Defined in this way, the demotic subculture also includes all the "dull" and most of the "artisan" families.

There was a gradient of increasing family size from "aspirant" through "rough" to "dull".

Further, among Roughts, occupations were often semi-skilled in small families, unskilled in large. Small families made little use of any type of agency and were suspicious of the research. Large families tended to have many agency contacts, particularly of the disciplinary type. They accepted the research, perhaps partly in order to placate authority. In these respects small "rough" families resembled "artisan" families, which were also relatively small.

It thus appears that important social differences are associated with family size. The Scottish Mental Survey showed that family size is related to measured intelligence; within each social class intelligence quotients were lower in large than in small families (Scottish Council for Research in Education, 1949). Our results suggest that these disparities in intelligence quotients may be related to social differences associated with family size.

"Dull" families have been regarded by some as a socially isolated and self-perpetuating group who tend to remain at the lowest social levels because of biological inferiority (Goddard, 1914; Lidbetter, 1933; Town, 1931). In our view, the situation is more complex and their social position is determined to a large extent by cultural and economic factors. In some cases there is evidence of a downward social drift, due to psychological or social causes. In others we found evidence of social rehabilitation, and some large families made recoveries at later stages when the children were grown and the family burdens lessened. Evidence on their intellectual development, which is presented in a later paper, supports the view that cultural factors play a part in their educational failures; it is to be expected that these factors would affect more than one family member.

It is important to note that the families described in this paper are not representative of working class families. Particularly in the case of the demotic subculture, it is not possible and may be dangerous to generalize from this sample of the educationally subnormal. It also needs to be borne in mind that cultures in industrial society are subject to change, and that young families may have changed already. "Aspirant", "artisan" and small "rough" families are probably a more representative group in local cultures than the large families.

This classification of families by occupation and education appears to have distinguished between social groups. In the papers that follow the classification

will be applied to describe some effects of social factors on the selection of children for special education and to examine effects of culture on intelligence. These additional results emphasize the distinction between the family groups.

SUMMARY

The families of young adults who had been ascertained educationally subnormal in Lancashire were classified by occupation and education. Four main types of family emerged, namely "aspirant", "artisan", "rough" and "dull". "Aspirant" families appeared to belong to an aspirant subculture which could be distinguished from the demotic subculture of the remaining families.

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FAMILIES OF DULL CHILDREN*

PART III.—SOCIAL SELECTION BY FAMILY TYPE

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IN this paper we have tried to demonstrate some of the ways in which social selection operates in the ascertainment of dull and subnormal children. In England backward children, by the terms of the Education Act of 1944, may be referred by their teachers for medical examination and "ascertained" as educationally subnormal, thereby qualifying for special educational treatment. Alternatively, they may be classed as mental defectives (or now, severely subnormal) and excluded from the schools altogether.

There are many reasons why children may be backward in school and unable to keep up with other children of the same age. They may suffer from brain injury or severe physical handicaps such as partial deafness or blindness. They may suffer from genetic or metabolic disorders, from cultural handicaps, from psychological disturbances, or they may simply lack intellect.

Thus one may classify the dull and the severely subnormal as being of two broad types, those that have lesions specific to mental deficiency and demonstrable clinically, pathologically, or biochemically; and those that do not have any demonstrable lesions.

For those that have no lesions various aetiologies have been postulated, which include genetic factors, hidden organic and metabolic factors, family deprivation and cultural deprivation. There is evidence which suggests that cultural and social factors are more likely to affect the mentally subnormal of high grade. Many patients of high grade have no demonstrable lesions, while those of low grade nearly always have demonstrable lesions (Crome, 1957). High-grade patients are found predominantly in the lowest social classes in contrast with low-grade patients who are discovered in all social classes (Paterson and Rundquist, 1933). Again, the high-grade among the subnormal are a marginal group, classified in some instances as dull normal, in others as educationally subnormal, and in yet others as feeble-minded; there is usually no difficulty in establishing the category of the low-grade or severely subnormal (Kirman, 1957).

The social factors may affect both selection and aetiology. In this paper we are concerned with the process of selection.

* This study was inaugurated by Professor C. Fraser Brockington, sponsored by the National Association of Mental Health, and aided by a grant from the Halley Stewart Trust to one of us (Z.A.S.). The Medical Officers of Health of Lancashire County Council (Dr. S. C. Gawne) and of Salford County Borough (Dr. J. L. Burn) made the survey possible by seconding field workers.

We postulated that the cultural milieu would enter into selection, i.e. the child from the lower social classes would be at a greater risk of ascertainment than his equally dull peer from higher social classes. We expected that a patient ascertained from a high social class would be of lower intelligence, or otherwise would suffer from brain damage or severe handicap.

METHOD

A random sample of 106 subjects aged 20–24 years who had been “ascertained” as educationally subnormal at school in Lancashire County and Salford City were followed up.

Their 102 families were classified into cultural groups as set out in a previous paper as follows:

- Aspirant Subculture: 9 Aspirant families.
- Demotic Subculture: 12 Artisan families.
56 “Rough” families.
25 “Dull” families.

It was intended to relate clinical with social data and therefore 50 subjects were examined. The four hour examination included the following items:

1. Medical history, social and psychiatric interview and physical examination.
2. Height, weight and subcutaneous fat measurements; photographs.
3. Special investigations: audiometry; urine tests for phenylketonuria and aminoacids; oral smear for sex chromatin; electro-encephalogram when the patient was able to attend a unit without losing working time (18 cases).
4. Intelligence test (Wechsler Adult Intelligence Scale) and Schonell reading test carried out by one of three trained testers. (A psychologist and one of us (Z.A.S.) tested 47 cases, a second psychologist tested the remaining three cases.)

When he made his examination the physician had no information about the social and psychological assessments. One of us, who administered about half the Wechsler tests, knew at the time part of the social case histories but none of the clinical data relating to the subject.

Selection of Examination Group

The selection of 50 cases for examination was influenced by three considerations.

1. *Family Type.* From the pilot study and a review of local records we guessed we would have very few subjects from “aspirant” families. We therefore tried to examine all such cases and succeeded in 7 out of 9.

We aimed at seeing half the “dysmorphic” cases to obtain a representative sample from this group and saw 10 out of the 22 subjects.

The complement was made up without prejudice from Artisans, Roughs and Dulls (33 cases).

2. *Locality.* Two of the nine Aspirants were omitted because their homes were too far distant (more than a day’s trip—including ferries).

“Dysmorphic” subjects were selected without regard to their accessibility, because they were a scattered group. The intended 50 per cent. sample was achieved after travelling as far afield as Crawley and Carlisle. There was a bias towards one mental deficiency institution in which 4 of our patients were confined; for convenience they were all seen on one expedition.

For the rest, consecutive cases were invited, starting in areas close to Manchester and gradually extending outwards, until we had gathered our full series. This procedure has not led to differences in geographical distribution between the family types.

3. *Refusals.* The examination was offered to 64 subjects selected on the above grounds and 14 refused. Almost all refusals came from small "rough" or "artisan" families.

Pre-knowledge. Preliminary medical information in our subjects was provided by reports made by school medical officers at the time of ascertainment. An analysis to check if cases had been selected because of known clinical problems revealed no such bias (Table I).

TABLE I

Neurological Lesions and Hearing Defects as Recorded at Ascertainment for Cases Examined, Refused and Not Invited (106 Cases)

	Cases Examined	Refused Examination	Not Invited	Total
Lesions noted at ascertainment	6	2	4	12
No lesions noted	45	13	36	94
Total	51	15	40	106

RESULTS

Clinical Classification

The 50 cases were classified as follows:

Positive Neurological Signs—5 cases (all of these had upper motor neurone lesions of varying severity and one also had epilepsy).

Epilepsy—3 cases (this number excludes the above patient with neurological signs and 2 imbeciles).

Imbeciles—7 cases (2 had epilepsy as well, and one other an abnormal EEG recorded from the cortex).

Hearing Defect—3 cases (only cases with bilateral loss of more than 40 decibels are included).

Abnormal EEG only—2 cases.

Clinically Normal—30 cases.

Imbeciles are almost always found to have brain lesions at autopsy (Crome, 1957).

The diagnosis of imbecility is not closely defined in the clinical literature or in the Mental Deficiency Act of 1913. Here the group labelled "imbecile" were all classed as "incomplete personalities" at the clinical examination. They were incapable of conversing and often made meaningless rejoinders, or responded to simple questions with "ask mum" or "I don't know". The rejoinders sometimes seemed to be parrot-like repetitions of parental injunctions, slogans and catch-phrases. Some had a degree of echolalia. These subjects often failed to name all their close kin and did not understand or participate fully in even the limited world of family and neighbourhood life. All had a transparent childlike emotional tone, and they were apprehensive and obviously fearful of the medical examination. In marked contrast with the remainder of our subjects, they were highly dependent on their immediate families in social matters and did not exercise average independence in their

daily lives, for example in making decisions about clothes, money, job-finding, holidays, entertainments and even friendships. None belonged to peer groups and none were married or had heterosexual relationships of any kind outside the kin group. These social and personal characteristics did not vary with the cultural milieu and the family type. All patients classed at the clinical examination as “incomplete personalities” were found to have I.Q.s of 55 or lower on psychological testing, and all patients with I.Q.s of 55 or lower on psychological testing had been clinically described as “incomplete personalities”.

The dividing line at about I.Q. 55 agrees with that of Larson and Sjogreh (1954) and is slightly higher than the tentative division at an I.Q. of 50 suggested by Penrose (1949).

Family Type and Clinical Status

Subjects from “aspirant” families form a different clinical group from subjects of other family types. All ascertained “aspirant” children had symptoms or signs of neurological damage or severe hearing defect, or an intelligence quotient at imbecile level with presumed neurological damage*. Children with such lesions were also found in the other family categories, but all the clinically normal children above imbecile grade came from the demotic subculture. The details are set out in Table II.

TABLE II
Fifty Cases: Clinical Type and Family Type

				Aspirant		Demotic			Total
						Artisan	Rough	Dull	
Neurological signs	..	..	1			1	2	0	5
Epilepsy	..	..	0			0	0	1	3
Imbeciles with lesions	..	..	1			0	2	0	3
Imbeciles without lesions	..	..	3			1	0	0	4
Severe hearing defect	..	..	1			0	2	0	3
EEG abnormality nil else	..	..	1			0	1	0	2
Clinically normal	..	..	0			3	13	7	30
Proportion with lesions	..	7/7				2/5	7/20	1/8	20/50

DISCUSSION

Two distinct social processes may contribute to this distribution of cases by family type. First, *social selection* for ascertainment and second the direct effects of *cultural milieu* on intelligence scores, educational performance, and possibly personality formation. (The effect on intelligence scores is the subject of a later paper.)

Several social factors affect the selection of children for ascertainment as educationally subnormal. Divergent local administrative practice leads to large differences between similar urban communities (Annual Report, M.O.H., Salford, 1957) and even within the same community; boys are ascertained more often and over a higher range of intelligence scores than girls; and children from “broken homes” and “dysmorphic” families not only appear to be more often ascertained, but are also more often admitted to mental deficiency institutions (Stein and Susser, 1960).

* The 2 “aspirant” subjects in the total sample of 106 who were inaccessible to clinical examination both appear to have neurological injuries. On family interview one is reported as having epilepsy, the other as having an “undeveloped left arm”.

Selection by social class and cultural background is illustrated by the material presented in this paper, which we interpret in the following way:

Children from the upper social classes would appear to avoid ascertainment altogether. We have no cases from Social Class I, and 3 per cent. from Class II.* In the Scottish Mental Survey of 6,000 children in 1947, Social Class I contributed 0.2 per cent. and Class II 3.4 per cent. of all school-children who scored less than the equivalent of an intelligence quotient of 85 to 86. Thus in any case there appear to be very few children in the ordinary schools with low scores in these social classes, but it is also likely that some outside of the ordinary schools escaped observation.

In the aspirant subculture only imbeciles and those with neurological injury and severe hearing defects were ascertained. In this group ascertainment may be seen as a means of circumventing the disparaging diagnosis of mental deficiency and at the same time of acquiring special educational treatment for the child.

In contrast, children from the demotic subculture who are ascertained include not only those with neurological injuries, hearing defects and low intelligence, but also children of higher intelligence without demonstrable physical lesions. Taking into account the stratification of our sample, we estimate that these clinically normal cases represent 75 per cent. of the total sample.

A presumption, based on the comparatively small number of imbeciles among demotic families, is that imbeciles from this group are more likely to be ascertained as ineducable, and excluded from any educational system, than are those from "aspirant" or professional families. In other words, the intelligence quotient thresholds for ascertainment as educationally subnormal and as ineducable are set at different levels for Roughs and for Aspirants. Thus in this sample the median intelligence quotient was 76 for Roughs and 55 for Aspirants.

Only the end result of the process of ascertainment has been examined. The last decision rested in the hands of a school doctor, and more or less legitimate social judgments must have entered into these decisions. But decisions had already been made about each child before it reached the school doctor, and had certainly limited his choice of action. Thus the teacher, who is perhaps more sensitive to community pressures than the doctor, first decides to draw the headteacher's attention to the backward child, and the headteacher decides whether or not to refer the child to the doctor.

Awareness of this process of social selection should make us look more carefully at the validity of many surveys of prevalence, genetic studies and clinical studies of mental subnormality. For example, estimates of prevalence are usually based on hospital and ascertained populations and therefore should reflect the bias in ascertainment and admission that has emerged in this study. Genetic studies are affected because selection by social factors may give the appearance of a familial incidence of mental subnormality in some social groups and not in others. Clinical studies may be affected in several ways.

* In the 1951 Census, the distribution of occupied or retired males between 15 and 65 by Social Class was as follows:

				Social Class Percentage				
				I	II	III	IV	V
England and Wales ..	..	..	3.3	15.0	52.7	16.2	12.8	
Scotland ..	..	..	3.1	13.0	51.3	18.3	14.4	
Lancashire County ..	..	..	2.3	12.7	53.1	14.8	17.1	
Salford County Borough ..	..	..	1.4	9.8	52.2	15.7	20.9	

First, it has been shown that the distribution of ascertained cases with and without organic lesions is related to selection by social factors. Second, the physique of ascertained cases is likely to be affected by the poor social environment, which favours their selection for ascertainment. Third, the psychological stability of ascertained cases and particularly hospital cases may be impaired by separations and other adverse childhood experiences which also favour their selection for ascertainment and for hospital admission (Stein and Susser, 1960).

It is evident from this investigation of the distribution of clinical types of subnormality in different subcultural and family groups that culture, social class and family function profoundly influence the diagnosis and management of the educationally subnormal child.

SUMMARY

The process of selection by social and clinical factors in the ascertainment of educationally subnormal children has been examined in a group of 106 subjects aged 20–24 years from 102 families in Lancashire.

Family types are distinguished from each other by occupational and educational criteria, and separated into two groups regarded as subcultural, viz., "aspirant" families from an aspirant subculture, and "rough", "dull" and "artisan" families from a demotic subculture.

In the two subcultural groups, the clinical status of the subnormal subjects is quite different.

All children ascertained from the aspirant group had symptoms or signs of neurological lesions, or severe hearing defects, or they were imbeciles with presumed neurological lesions. Children with such lesions were also found in the demotic group, but all the clinically normal children who were of higher intelligence came from the demotic subculture.

This distribution of clinical types is partly due to selection for ascertainment by social class and cultural background, a process which may affect the validity of many epidemiological, genetic and clinical studies of mental subnormality.

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APPENDIX A

Clinically Normal, Demotic (30 Cases)

(Excludes 1 case for whom no W.A.I.S. obtained)

Case No.	T.M.*	Age	R.M.*	W.A.I.S.	W.A.I.S. -T.M.*	W.A.I.S. -R.M.*	Test-Retest Interval (Years)	Family Type
1	71	13	76	79	+8	+3	10	Dysmorphic
2	57	15	58	62	+5	+4	7	Dysmorphic
3	62	9	66	75	+13	+9	16	Dysmorphic
4	71	14	73	73	+2	+0	7	Dysmorphic
5	51	16	56	62	+11	+6	9	Dysmorphic
6	74	13	79	90	+16	+11	8	Dysmorphic
7	74	12	80	77	+3	-3	13	Dysmorphic
8	77	16	80	78	+1	-2	5	Deviant
9	68	16	69	81	+13	+12	12	Deviant
10	62	12	70	68	+6	-2	12	Deviant
11	73	13	78	77	+4	-1	11	Deviant
12	66	11	73	77	+11	+4	14	Dull
13	85	7	85	88	+3	+3	17	Dull
14	73	13	78	85	+12	+7	12	Deviant
15	74	13	78	81	+7	+3	11	Rough
16	61	12	69	76	+15	+7	10	Rough
17	68	12	75	81	+13	+6	9	Rough
18	63	15	64	75	+12	+11	9	Rough
19	84	9	86	95	+11	+9	7	Rough
20	64	14	69	90	+26	+21	16	Rough
21	67	13	73	74	+7	+1	9	Rough
22	80	7	80	90	+10	+10	18	Rough
23	83	7	82	84	+1	+2	17	Rough
24	75	13	77	86	+11	+9	12	Rough
25	62	14	65	81	+19	+16	11	Rough
26	74	14	76	72	-2	-4	10	Rough
27	68	12	75	76	+8	+1	13	Rough
28	68	12	75	76	+8	+1	12	Rough
29	73	11	83	66	-12	-17	11	Rough
30	73	9	76	79	+6	+3	13	Rough

Mean Scores for Group	70.2	12.2	74.13	78.46	+8.26	+4.33	11.1	
S.D. for Group	8	2.6	7	7	6.8	7	3.4	

T.M. = Terman-Merrill.

R.M. = Terman-Merrill scores corrected by Roberts-Mellone method.

W.A.I.S. = Wechsler Adult Intelligence Scale.

APPENDIX B

Brain Injured (Demonstrated or Assumed) E.S.N.s (16 Cases)

(This excludes 3 partially deaf and 1 misdiagnosis)

Case No.	Diagnosis	T.M.	Age at Testing	R.M.	W.A.I.S.	W.A.I.S. -T.M.	W.A.I.S. -R.M.	Test-Retest Interval (Years)	Family Type
4	Imbecile and abnormal EEG	70	13	75	53	-17	-22	10	Aspirant
35	Imbecile	49	8	52	51	+2	-1	15	Aspirant
36	Imbecile	57	9	61	55	-2	-6	12	Aspirant
37	Abnormal EEG	76	10	80	78	+2	-2	11	Aspirant
38	Upper motor neurone lesion	70	12	76	87	+17	+11	11	Aspirant
39	Imbecile	63	10	69	51	-12	-18	13	Aspirant
40	Epilepsy	83	8	84	72	-11	-12	17	Dysmorphic
41	Epilepsy, upper motor neurone lesion	63	10	69	67	+4	-2	11	Dysmorphic
42	Epilepsy	75	11	78	76	+1	-2	14	Dysmorphic
43	Imbecile	55	7	53	55	0	+2	17	Rough
44	Upper motor neurone lesion	69	10	74	59	-10	-15	13	Rough
45	Epilepsy	83	11	87	84	-1	-3	12	Dull
46	Upper motor neurone lesion	73	10	77	69	-4	-8	14	Rough
47	Epilepsy	46	13	56	47	+1	-9	11	Rough
48	Abnormal EEG	86	9	88	106	+20	+18	16	Rough
49	Epilepsy	50	9	55	40	-10	-15	13	Rough
Mean Scores for Group		66.75	10	70.9	65.6	-1.25	-5.25	13.1	
S.D. for Group		12	1.7	12	17	9.9	10.3	2.2	

APPENDIX C

Clinically Normal Apart from Severe Hearing Defects

Case No.	Diagnosis	T.M.	Age at Testing	R.M.	W.A.I.S.	W.A.I.S. -T.M.	W.A.I.S. -R.M.	Test-Retest Interval (Years)	Family Type
31	Otitis media	66	13	72	73	+7	+1	10	Rough
32	Otitis media	60	7	58	75	+15	+17	18	Rough
3	Otitis media	63	7	62	Scored 70 on Matrices test	—	—	17	Aspirant

FAMILIES OF DULL CHILDREN*

PART IV.—INCREMENTS IN INTELLIGENCE

By

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THIS paper deals with some effects of family and culture on intelligence, as studied in a sample of 50 young adults who had been ascertained as educationally subnormal at school.

The high prevalence of dullness among the unskilled suggested to Lewis the existence of a subnormal culture† (Lewis, 1933). The sharp decline in the prevalence of recognized cases with age (Penrose, 1954), the social recovery in adulthood of cases apparently defective in childhood (Doll, 1947; Cassel, 1949) and particularly, the increments in intelligence made by adults with poor family backgrounds in mental deficiency institutions (Guertin, 1949, 1950; Clarke and Clarke, 1954) indicate that certain groups among dull or subnormal patients may make intellectual and social advances in adulthood.

In this investigation, the postulate was made that such advances might be expected in those educationally subnormal subjects who came from sub-cultural groups which provided few incentives, opportunities and facilities for intellectual achievement. In an earlier paper, a group of the educationally subnormal had been identified as belonging to a subculture of this type which was termed demotic.

It was also postulated that the greatest advances would be made by the educationally subnormal of higher intelligence who had no detectable neurological lesions, a group which had been found only in this demotic subculture.

In the educationally subnormal of low intelligence (imbecile level) or with neurological lesions, it was expected that advances would be small or would not occur, in accord with the usual expectation in mental subnormality. But it was thought that the brain-injured from the demotic subculture might make gains in comparison with those from the more favoured subcultural group described as aspirant.

METHOD

In order to test these hypotheses it was necessary to follow up educationally subnormal subjects, to distinguish subcultural groups among their families,

* This study was inaugurated by Professor C. Fraser Brockington sponsored by the National Association of Mental Health, and aided by a grant from the Halley Stewart Trust to one of us (Z.A.S.). The Medical Officers of Health of Lancashire County Council (Dr. S. C. Gawne) and of Salford County Borough (Dr. J. L. Burn) made the survey possible by seconding field workers.

† Subculture, which is the word he used, has a different meaning in current technical usage.

to examine them clinically, and to compare their present intellectual performance with performance in childhood.

A stratified sample of 50 subjects aged 20-24 years, all of whom had been ascertained as educationally subnormal at school, was selected for study and their families were classified into demotic and aspirant subcultural groups by occupational and educational criteria. The families of upbringing of those from the demotic subculture were categorized as "rough"*, "dull", "deviant" or "dysmorphic", those from the aspirant subculture as "aspirant". The details of method, sampling and family classification are set out in the first two papers in this study (Stein and Susser, 1960).

All these subjects were tested on the Wechsler Adult Intelligence Scale at the time of clinical examination. Their scores were compared with their previous scores on the Terman-Merrill test given at the time they were ascertained as educationally subnormal at school. Where there was more than one school test, the highest score was used.

The Terman-Merrill tests were given by educational psychologists and school medical officers, all of whom were approved for this work by the Ministry of Education, but who came from different parts of the county. Although the standards of testers may have varied, individual bias on their part should not affect results for groups of cases distributed evenly between them.

The school tests were given at ages ranging from 7 to 16 and averaging 11 years. This might introduce error into comparisons of results, since the standard deviations for the Terman-Merrill tests are not the same at all ages, while the standard deviation for the Wechsler Adult Intelligence Scale is 15 at all ages. For this reason, the Roberts-Mellone corrections have been applied to the Terman-Merrill scores to make these conform with tests giving a standard deviation of 15 at each age (Roberts and Mellone, 1952). Both corrected and uncorrected scores have been compared with the adult Wechsler scores.

RESULTS

Details of individual test scores, age at testing and time intervals between school and adult tests, are set out in the Appendix.

Sixteen subjects, all the six from the aspirant subculture and 10 from the demotic subculture, had some evidence of neurological lesions (Table I)†. This number includes four cases with the intelligence and clinical features of imbeciles, but without clinical signs of neurological damage.

At autopsy 92 per cent. of imbeciles have been found to have lesions of the brain (Crome, 1957) and therefore imbeciles have been regarded as having presumptive evidence of such lesions. In this paper these 16 cases with evidence of neurological lesions will be termed brain-injured.

Thirty subjects are described as clinically normal. This excludes three cases with severe hearing defects due to middle ear disease‡. Their inclusion

* Families classed as "artisan" in Part II are here included with "rough" families.

† This number excludes one case with a neurological lesion in the demotic group. He was patently misdiagnosed; he had had no schooling when first tested on entrance to a secondary modern school at twelve years of age, but had graduated from the backward to the top class of the school by fifteen years of age. He now does mathematics for pleasure, and has a W.A.I.S. score of 114.

‡ Two were of the demotic and one of the aspirant group. Results for these cases are included in the Appendix. The handicap of the case from the aspirant group was so severe that Raven's matrices had to be substituted for the W.A.I.S.

TABLE I

Subjects with Neurological Lesions Classified by Clinical Type and Subculture
(16 Cases)

	Aspirant Subculture	Demotic Subculture	Total
Neurological signs	1	3	4
Epilepsy	0	3	3
Imbeciles with lesions ..	1	2	3
	(cortical lesion)	(both epileptics)	
Imbeciles without lesions ..	3	1	4
EEG abnormality only ..	1	1	2
Total	6	10	16

in the body of the paper would not alter the reported results, but it was judged wiser to avoid the further variable introduced by their hearing handicaps. Another clinically normal case with an I.Q. gain of 24 points was excluded because we did not administer the adult test ourselves.

I.Q. Changes by Clinical Status (Table II)

TABLE II

I.Q. Changes by Clinical Status

(a) Wechsler Adult Score Compared with Uncorrected Terman-Merrill Childhood Score

Clinical Status	Increments	Unchanged*	Decrements	Total Cases	Mean Change [(points)]
Normal ..	23	6	1	30	+8.3
Brain injured ..	3	7	6	16	-1.2

(b) Wechsler Adult Score Compared with Terman-Merrill Childhood Score Corrected by Roberts-Mellone Tables

Clinical Status	Increments	Unchanged*	Decrements	Total Cases	Mean Change (points)
Normal ..	15	13	2	30	+4.3
Brain injured ..	2	6	8	16	-5.25

* Unchanged means within ± 3 points of the original score which is the standard error of the mean for the group.

Clinically normal subjects make a mean gain of 8.3 points when their childhood scores on the Terman-Merrill are compared with their adult scores on the Wechsler; brain-injured subjects show a mean loss of 1.25 points when their results on these two tests are compared.

Clinically normal subjects make a mean gain of 4.3 points when childhood scores on the Terman-Merrill corrected by the Roberts-Mellone tables are compared with adult scores on the Wechsler; brain-injured show a mean loss of 5.25 points when corrected scores are compared with Wechsler scores.

For either corrected or uncorrected Terman-Merrill scores, the brain-injured score 3.3 points lower than the clinically normal in childhood, and 13 points lower on the adult test.

Testing the difference in increments between clinically normal and brain-injured subjects, using the corrected scores for the comparison, the *t* test gives $t=3.73$ with 44 d.f. ($P=0.002$).

Table II shows the mean results and the numbers of individuals who made increments and decrements for each group.

Next we considered I.Q. changes by clinical status within a single subculture. Increments made by clinically normal and by brain-injured subjects were compared taking the demotic group alone. Testing the differences between these groups by the *t* test, $t=3.14$ with 38 d.f. (*P* is less than 0.01), using the corrected scores for the comparison.

Comparisons of scores on verbal and performance tests and on subtests of the Wechsler did not reveal differences between the clinically normal and the brain-injured.

I.Q. Changes by Subculture (Table III)

TABLE III

I.Q. Changes by Subcultural Group and Clinical Status

(Wechsler Adult Score compared with uncorrected Terman-Merrill Childhood Score)

Subculture	Increments	Unchanged	Decrements	Total Cases	Mean Change
Demotic (clinically normal)	23	6	1	30	+8.3
Demotic (brain injured) ..	2	4	4	10	-1
Aspirant (all brain injured)	1	3	2	6	-1.7

For simplicity only uncorrected scores are discussed in what follows.

Among the *brain-injured*, no differences could be shown between those from the demotic and those from the aspirant subculture. Neither group made gains. However, the numbers are small.

For the *clinically normal*, who came only from the demotic subculture, no comparisons could be made.

I.Q. Changes by Family Type (Table IV)

TABLE IV

I.Q. Changes in Clinically Normal Subjects by Family Type

(Wechsler Adult Scores compared with uncorrected Terman-Merrill Childhood Score)

Family Type	Increments	Unchanged	Decrements	Total Cases	Mean Change
Dysmorphic ..	5	2	0	7	+8
Dull ..	5	2	0	7	+7
Deviant ..	4	1	0	5	+9
Rough ..	13	2	1	16	+9

Subdivision of the *brain-injured* cases of the demotic group into dysmorphic, dull and rough families yielded groups too small for valid comparison.

Among the *clinically normal*, breakdown by family type revealed no differences, although the size of the family subgroups may have been too small for slight differences to emerge.

The thirty clinically normal cases were grouped as follows:

Dysmorphic Families (7 cases)

Five had made gains in adult intelligence scores, two had remained the same and none had deteriorated. The mean gain was 8 points.

Dull Families (7 cases)

Five had made gains in adult intelligence scores; two had remained the same and none had deteriorated. The mean gain was 7 points.

Among these seven subjects were five whose families had been categorized in a previous paper as *deviant* (Stein and Susser, 1960). (Deviant families had transgressed those standards of child care legally enforced by the N.S.P.C.C. and School Attendance Officers.) Of these subjects, four had made gains in adult intelligence scores, one had remained the same and none had deteriorated. The mean gain was 9 points.

Rough Families (16 cases)

Thirteen had made gains in adult intelligence scores, two had remained the same and one had deteriorated. The mean gain was 9 points.

DISCUSSION

Changes in intelligence quotients among a sample of young adults who had been ascertained educationally subnormal at school have been grouped first according to clinical status, second according to subcultural group and third according to the type of the family of upbringing. Cases similar to the educationally subnormal may sometimes be classed as dull, and sometimes as high-grade feeble-minded, and our results may be applicable to both these groups.

Clinical Status

As a group clinically normal cases have made significant gains in intelligence as compared with their own childhood scores, and with the childhood and adult scores of brain-injured cases. The intelligence of brain-injured cases has remained the same as in childhood. Results based on the Roberts-Mellone corrections suggest another less likely interpretation. It may be that the clinically normal have improved rather less, but that the brain-injured have markedly deteriorated. Either way, this may be taken as an indication of a real difference between the clinically normal and the brain-injured. Previous research aimed at demonstrating such a difference has usually relied on special psychological tests (Strauss and Lehtinen, 1951). The results are not widely accepted (Sarason, 1953; O'Connor, 1958).

Subcultural Groups

Proof that increments in adult intelligence among the educationally subnormal are due to cultural factors requires comparison between subjects from different cultural groups.

Brain-injured cases were found in both demotic and aspirant subcultures, but the gains were the same in both groups. This similarity may be determined by the brain injury itself. Possibly these cases are less responsive to environmental stimuli.

Clinically normal subjects were found only in the demotic and not in the aspirant subculture, and as a result we do not have direct evidence that the gains in measured intelligence made by the clinically normal are due to cultural factors. Nevertheless, we do have indirect evidence on this point.

No clinically normal cases were discovered from the aspirant subculture or from higher social classes. In part this distribution may be attributed to selection by social factors (Stein and Susser, 1960). However, in the Scottish Survey of National Intelligence also, very few low scorers were found in the

higher social classes although many were found in the lower social classes (The Scottish Council for Research in Education, 1953). It does not appear that social selection could account for the whole of this result since 11-year-old children from the great majority of schools participated in the Scottish survey. Results from the present investigation indicate that many of the low scorers in the lower social classes are likely to be clinically normal and that such cases are rare in the higher social classes. It may therefore be inferred that the low scores of normal children from the demotic subculture are lower than those of normal children from other cultural groups.

Much indirect evidence suggests that a poor cultural environment is conducive to lowered scores on intelligence tests (Sarason and Gladwin, 1958). In addition, the work of Luria and of Kirk has demonstrated the importance of environmental stimuli in the development of young retarded children (Luria, 1958; Kirk, 1958). The demotic subculture, poor not only in goods but in language and intellectual concepts (cf. Bernstein, 1958) might thus be expected to depress I.Q.s in childhood.

It appears from our study that increments occur in a specific subculture but not in the population as a whole. This may be assumed because intelligence tests in childhood ranked the demotic clinically normal group higher, in relation to the general population, than did childhood tests. Thus the demotic subculture common to this group is likely to be related to the rise in their intellectual rank as adults although it is conceivable that genetic or nutritional or other factors might contribute to this result. Cultural influences presumably retard intellectual growth in these children, but some of the deficit is made up with maturity.

We may suspect that together with social and administrative readjustments (Susser, 1959) this gain in measured intelligence contributes to the apparent decline in the incidence of mental deficiency with age (Clarke and Clarke, 1959).

Disturbed Family Background

Clarke and Clarke (1953) have previously demonstrated significant increments in I.Q. made by a group of adults, classed in a mental deficiency institution as high-grade mental defectives. Their work pointed to disturbed family background as an influence which had retarded intellectual maturation. In this study we have distinguished two kinds of disturbed family background, namely dysmorphic and deviant.

Dysmorphic families had failed to provide their members with a set of enduring human relationships in the early years of life, so that at some time subjects from these families had all lived in institutions or foster homes. Deviant families showed signs of social disturbance in that they had been subject to the action of those agencies which apply legal sanctions for neglect in child care and school attendance.

Gains made by subjects from these two types of family were the same as those made by other groups from the demotic subculture. Thus disturbance in the family of upbringing did not modify the gains in intelligence among clinically normal subjects, although it may have contributed to their initial intellectual retardation.

These gains are less than those reported by Clarke, Clarke and Reiman (1958). In their series, subjects continued to make gains over an observation period of 6 years, at the end of which the average age was over 25 years. Our subjects have perhaps not yet attained their peak scores.

Dullness in Families

Dull families are those in which at least one child besides the *propositus* had been officially ascertained as educationally subnormal or mentally defective. These included the five deviant families. The increments in I.Q. for the seven clinically normal cases from the eight "dull" families were the same as for the remainder of the clinically normal. Thus cultural factors probably affected these cases in the same way as they did other clinically normal cases.

Comparability of Tests

The increments in I.Q. scores made by clinically normal subjects appear to be real gains that do not reside in the nature of the tests used.

It has been thought that the Terman-Merrill test might be more affected by cultural factors than the Wechsler (Clarke and Clarke, 1958). The scores of brain-injured cases from both cultures were consistent on the two tests, however, indicating that the tests are comparable in the circumstances of this investigation. They have previously been found comparable in a study of educational backwardness (Collins, 1956).

Measurement Error

The increments in clinically normal cases represent a regression to the mean. Although in small part this regression may be due to measurement errors, our interpretation is that in the main it is due to retarded intellectual maturation in these dull children.

CONCLUSIONS

Two distinct types of case, the brain-injured and the clinically normal, are found among subjects ascertained educationally subnormal.

The *brain-injured* have definite or presumptive evidence of neurological injury, may be drawn from either a demotic or aspirant subculture, and their intelligence when measured in adulthood appears to be the same as in childhood. It is presumed that such cases may be found in any subcultural group (although they are possibly less common in good social conditions than in poor ones (Knobloch and Pasamanick, 1958)) but that most such children from the higher social classes escape the administrative net of ascertainment.

The *clinically normal* have no evidence of neurological injury; in this sample they are drawn only from the demotic subculture, and they make intellectual gains when followed into adulthood. We calculated that such cases comprised 75 per cent. of the total sample. This distribution appears to be in part the consequence of a retardation in intellectual growth due to cultural influences.

Thus the prognosis for intellectual advance is better for the clinically normal from the demotic subculture than for the brain-injured. The presence of gross brain-injury can be identified with reasonable accuracy by clinical means, and the subcultural type of a particular family by a systematic social history.

Although the assessments in this study were made in adults, it might be possible to make a reasonable prediction in childhood as to outcome in individual cases of the types found in this sample.

SUMMARY

The effects of family and culture on intelligence have been studied in a sample of 50 young adults who had been ascertained as educationally subnormal at school.

As a group, clinically normal subjects made I.Q. increments whereas subjects with definite or presumed neurological lesions did not make increments. This may be taken as an indication of a real difference in intellectual potential between the clinically normal and the brain-injured in this group of the educationally subnormal.

Seventy-five per cent. of subjects ascertained educationally subnormal were clinically normal and all these were of the demotic subculture. The increments they made in I.Q. appeared to be due to cultural factors which had retarded intellectual maturation.

Disturbances of family background did not alter the size of I.Q. gains made by clinically normal subjects of the demotic subculture.

Cases in which there was familial dullness, many of whose families in this sample were also deviant, made increments as did other clinically normal cases. They therefore appeared to suffer from cultural effects in the same way as did other clinically normal cases.

The increments in I.Q. scores made by clinically normal subjects appear to be real gains that do not reside in the nature of the tests used.

On the basis of these findings it might be possible to make a reasonable prediction in childhood as to outcome in individual cases.

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ON OPENING AN ADOLESCENT UNIT*

By

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THE main purpose of this paper is to report our experience in developing a psychiatric in-patient unit for adolescent boys. The Unit is known as Beech House and contains 16 beds and has been operating since January, 1959. It is a non-statutory ward and is the first treatment unit of this kind attached to a large provincial mental hospital such as St. Augustine's. Its catchment area is limited to the South-East Metropolitan region which comprises Kent and part of East Sussex. Only exceptionally are cases from outside these two counties accepted into the unit.

The present trend in this country is to open more of such units for the residential treatment of adolescents and the observations that we have made in the first nine months of the Unit's existence may be of interest to those who will be engaged in similar work in future. I shall describe the original blue-print and then point out the various modifications that had to be made. I shall deal essentially with changes of policy as they affected the administrative and therapeutic structure of the Unit.

DESCRIPTION OF WARD

The first main problem that we had to solve was one of planning. The Unit is housed in two villas situated at the periphery of the hospital estate in nearly open country with a few adjoining woods. These twin buildings, two storeys high, were originally designed to be self-contained wards. They were not altogether suitable for our purpose and had to be structurally altered to suit our needs. The Hospital Nurses' Training School is housed on the ground floor of one of these villas, and only the first floor is available to us. Ideally we should have preferred one large self-contained ward equipped to serve the needs of 16 in-patients rather than two separate buildings. The school, considered very much as a link with the outside world, would have been better placed in a building set apart on its own. "Going to school" would then have approximated more closely to the routine experience of ordinary schoolboys. We had to make the best of the available accommodation and eventually we decided to use the one whole villa allocated to us as the main living centre during the day. The school became included in it.

The ground floor comprises a large dining room and a common room equipped with table tennis, billiards and television set. The doctor's clinic, charge nurse's office and kitchen are also situated on this floor. The first floor, formerly a large dormitory, has been altered to include the school as well as separate rooms for the therapist, the P.S.W. and the teacher. Rooms have been

* This talk was given at the South-Eastern Divisional meeting of the R.M.P.A. at St. Augustine's Hospital, on 7 October, 1959.

set aside for various activities such as carpentry and clay-modelling. One room is also available on this floor for the temporary seclusion of very disturbed patients.

One disadvantage resulting from the close proximity of the school to the ward is that no safe curtain exists to prevent the spill-over of negative reactions from one quarter to another. It is more difficult, for instance, for the anxious child who acts out aggressively in the school to feel safer in the ward when one is a mere extension of the other. In this way, aggressive reactions in too confined premises tend to diffuse very widely because adults become closely identified with one another.

The sleeping quarters are situated on the first floor of the other villa, known as "Redwood". There are 10 individual bedrooms and a 6-bedded dormitory reserved for newly admitted boys. Individual rooms are allocated by order of seniority or merit. A fairly large assembly room is used in the evening by boys who wish to watch television programmes. I must confess that this television set was originally placed there to induce our patients to move over to their sleeping quarters without murmur. The idea has worked out fairly well. Only the more senior boys are allowed to sit up late to watch T.V. programmes of special interest. Normal lights out is at 10 p.m. The remoteness of the sleeping quarters from the ward has had many disadvantages. There is no supervision there during the day and for this reason the boys are not allowed to go to their room. Some have undoubtedly resented this lack of privacy, particularly when they wanted to isolate themselves from the group.

STAFF ORGANIZATION AND AIMS

The organization of such a unit must be flexible enough to meet quite widely divergent needs; it must accommodate the youngster who has made a psychotic type of withdrawal as well as the child who is passing through a phase of acute acting-out and presents severe behaviour problems. This necessitates the combination of the special educational techniques of the schools for maladjusted children with the psychiatric and nursing techniques developed from experience in mental hospital care.

Our primary aim in such a unit is to modify the more grossly pathological defences. The child who, through his own insecurity and inadequacy, has drifted too far into a world of fantasy and fears reality, needs a community in which he can gradually learn to act out and find satisfaction in day to day living.

The staff comprises the physician in charge, who supervises the administration and clinical aspects of the Unit. He has under his direction a full-time male therapist who co-ordinates individual and group therapy programmes. Stress is laid on environmental therapy which is based upon the therapist, teachers and nursing staff working as a team. Regular meetings are held in which observations are shared and attitudes to the patients discussed. A diagnostic conference is held on every new case one month after admission. Observations and opinions from all the members of the Unit, are pooled and a collective decision made regarding future therapeutic procedure.

The nursing staff consists of two charge-nurses, two male staff-nurses, two female assistant-nurses and two student nurses. They rotate every eight hours in shifts. Two nurses are on duty at night between 8.30 p.m. till 7 a.m.

The nurses' duties most nearly correspond to those of parents. They attend to the patients' material needs, but are also closely involved with them in the day to day living situation. They participate actively in recreational activities

with them and try to provide the authority and affection of parental figures. Female nurses have been accepted as mother figures and one middle-aged nurse has succeeded particularly well in this task.

It was soon noticed that the greatest call on the resources of the nurses came in the evening period after 6 p.m. when organized activities and psychotherapy have ceased. This is the time when normally at home, family life comes into its own. It is perhaps ironical to say that at the Unit it is often a time of strife! This period brings with it what is probably the nearest approximation to the home situation. Old anxieties and aggressive responses are reactivated and readily give rise to rebellious behaviour patterns in some boys, whilst others manifest their dependency needs by their increased attention-getting behaviour with adults. To alleviate the nurses' task we have organized recreational and social activities on several evenings during the week.

The Unit cannot be run in isolation from the outside social environment as in the most conventional type of adult psychiatric ward. The Psychiatric Social Worker is therefore primarily employed in maintaining close links between the patient and his family. By regular home visits, as well as interviews at Beech House, the parents are brought into the therapeutic situation as much as possible. We also aim to maintain contact with the referring clinic and get their co-operation over family case work.

The school is under the control of the Kent Education Committee which supplies the two teachers attached to the Unit. The boys spend four hours in the school each day from Monday to Friday. They are divided into groups and receive individual attention. The school programme is extremely flexible and varied and aims to be therapeutic as well as educative. The teacher's approach is guided by the level of emotional disturbance in each boy rather than by the level of scholastic attainment.

CHANGE IN CONCEPTS

Since the unit opened some of our original concepts have had to be significantly modified. We started with the premise that permissiveness should be the governing principle underlying our attitude to the patients. We inferred that controls should be reduced to a minimum and instituted the open door policy as it is applied to most of the wards in the hospital. We soon found that we were left by ourselves in the ward whilst our patients roamed freely about and committed an increasing number of destructive acts in the vicinity. The Unit seemed to have no other function to them but to provide food and shelter. The greater freedom they enjoyed the less inclined they were to become involved with us.

A crisis was soon upon us when a small rebellion suddenly broke out. The leader was an aggressive psychopathic boy who persuaded a group of patients to accompany him to a near-by wood. He and his retinue refused to return to the ward and slung abuse at the nurses. All seemed greatly encouraged by their leader who brandished a 6-inch self-made dagger and blustered threats. With approaching darkness the situation grew more enervating for the staff, who felt powerless. However, with skilful manoeuvring the group was split, its leader isolated and the rebellion brought under control. Needless to say we had to take notice of this rather ugly reality situation and limit our patients' freedom. It almost seemed as if the Unit's survival was at stake. The open door became the half closed door, no boy was allowed out without escort unless he could be trusted and indicated beforehand where he wanted to go. Anyone guilty of an

offence outside the Unit automatically became gated. This form of sanction re-established confidence and security in the staff and patients.

Analysis of the situation suggests that the crisis could be attributed to three sets of factors. In the first instance the group contained too high a proportion of aggressive boys with delinquent tendencies. In future a more discriminate selection would be required and no more than two or three dissocial boys admitted at any one time. Secondly, it must be remembered that the staff had only just come together to form a new team. Some had only just met and were therefore untried and unaccustomed to one another, the majority were inexperienced with the residential treatment of adolescents, all were anxious and relatively untrained in their new position. In the case of the nurses few were able to act spontaneously in situations demanding immediate intervention. It is no use waiting for doctor's orders when a boy breaks a window. The very word permissiveness in many instances seemed to inhibit the nurses and one could undoubtedly speculate with interest on its various interpretations. It is a fact that in the early days of the Unit permissiveness was understood to mean an attitude of benevolent neutrality, its application sometimes demanding an almost masochistic sense of leniency. This fits in with the traditional role of the mental hospital nurse who is trained to be a passive observer with custodial duties in adult psychotic wards. Nothing could be more phoney to adolescents, who need to feel that adults in charge of them can experience appropriate emotional responses and are not afraid to show disapproval if necessary when wilfully defied. This is what a normal child expects from his parents and indeed the basis of any identification with the parents must be the truthfulness and predictability of parental responses. For it is only then that a child will begin to accept and respect their authority. Perhaps our greatest mistake when we started was to ignore our patients' profound need for parental attitudes from us and their relative indifference to our good sibling-like comradeship. They need to be guided as well as sympathetically treated.

Our good intentioned attempt to institute a profoundly liberal regime had the effect of plunging a group of disturbed adolescents into a structureless society in which there was no effective authority and therefore no adequate safeguards against their own destructive impulses. The rebellion certainly provoked adults in charge into showing their authority by re-establishing some controls without which our patients did not feel secure.

Sensing our passivity as an anachronism our rebels quickly forced us back into realistic parental roles. It is perhaps characteristic that all the time the Unit was wide open the usual reaction of the boys to our approach was one of flight. "Running out to the wood" became a familiar pattern and our contact with our patients deteriorated into a vast game of hide and seek. Our patients refused to get involved personally with us unless we could show them we were masters in our own house.

DISCUSSION

Adolescence, the so-called "awkward age", is often regarded as an abnormal phase of normal development. The rising generation causes resentment, conscious or otherwise, in adults who know they will eventually be displaced. As a result the balance between parental authority and the adolescent's longing for independence is a very delicate one. Each adolescent necessarily seeks to throw off his dependent status by rebelling against parental controls. He is as yet unable to assume all the responsibilities of adulthood and can therefore

only aspire to gradual emancipation. Too restrictive management will drive him to open rebellion, on the other hand, full freedom is not yet acceptable to him and he will either provoke the re-imposition of adult controls or build rigid authoritative group structures for himself as the study of juvenile gangs shows.

It seems that the regime best suited for adolescents in a residential treatment centre is one of benevolent autocracy. Adult authority becomes acceptable if tempered with liberal measures. It must be firm but friendly. The chief authoritative figure, who is in effect the psychiatrist, imposes an ordered life routine in the unit as well as certain controls, e.g. prohibition to go out without permission or compulsory school attendance, but at the same time he also makes large concessions by allowing for instance unrestricted smoking or late bedtime.

An interesting experiment took place when we tried to introduce group debates by inviting our patients to form their own ward council. We had hoped that group tensions and latent aggression would have been successfully ventilated. The patients elected their own committee and agreed to have a non-voting member from the staff. Topics for debate (such as their opinion on the internal organization of the Unit) were suggested at first with the hope that it would lead our patients to talk about themselves spontaneously as in group therapy sessions. Our experience was different to what we had anticipated. The more assertive members of the group monopolized the debates whilst the rest, particularly the younger patients, remained passive. The debates deteriorated into battles of words between the boys' spokesman and the staff. Demands for more and more privileges were produced with each new meeting. As many of these as possible were granted but when they could not be satisfied this seriously aggravated tension in the group and caused wild diffusion of aggression which had delayed disruptive effects throughout the Unit. We had expected a calmer and more manageable group but instead we found ourselves faced with greater behaviour problems within the group. Eventually the meetings were discontinued and group anxiety decreased.

Many factors were probably at work in making this experiment a failure. If we had persisted the outcome might have been very different and we might have had a more constructive response eventually. So often adolescents act out their past experiences in the present situation and swing between acceptance or rejection of the adult. Hostility follows phases of enthusiasm and co-operation. However, the offer of self-government by a ward council seemed to have been interpreted at the time as a surrender of authority on our part. It caused considerable anxiety in the group. It also created a power vacuum which was exploited by potential group leaders who tried to establish their supremacy over abdicating father figures.

I think the question could well be asked whether a hospital community with its complexities and limitations is the right place for the treatment of disturbed adolescents. Mental hospital regime does not lend itself readily to the particular problems of that age group. Traditionally the excitable or aggressive patient is isolated and restrained or symptomatically treated by means of heavy sedation or E.C.T. The hospital environment is not designed to tolerate much of the aggressive acting out that is so common with adolescence. The attitude of the administration is for a safe group organization and its natural reaction to destructiveness is to demand adequate safeguards. The interests of other hospital departments are at stake just as much as the good name of the hospital in being able to protect the property of our neighbours. For these reasons the environment can never be as simple or free of restrictions as one would like it to be. The danger lies in introducing an atmosphere of

repression and institutionalization for safety's sake, when only the progressive experience of freedom can lead to emancipation and responsible behaviour.

A hospital ward can never become a home. Its contribution must therefore be in short-term adjustment, the emphasis being on providing a therapeutic experience rather than on meeting primary needs in the reality day to day situation. This necessarily curtails our choice of cases, since we cannot take the place of foster parents or offer long-term residential placement to those patients with severe dependency needs. In this respect we can only be of limited value to the bulk of the children who come to the notice of the Children's Department. The disposal of these cases is often difficult and our work is considerably hampered at times by the absence of a suitable half-way house to which our patients could be transferred before they are discharged. A hostel for maladjusted children attached to the unit would serve this purpose admirably. It would provide a suitable environment in which to unload cases requiring long-term residential therapy. It could also be an alternative to those patients whose home situation militates against their adjustment and maturation.

Perhaps one of the greatest drawbacks to the treatment of children in hospital is the absence of continuity of relationships with the nurses. Every eight hours a new shift takes over and the patient is faced with a situation to which he may react as if it were repeated desertion. His attempts to form lasting relationships with adults are constantly being undermined and may lead him to react aggressively against those adults by whom he feels rejected.

Nursing organization in the ordinary mental hospital is planned along rigid traditional lines to suit the needs of a large collectivity. It cannot be substantially modified to fit the requirements of one particular ward. We borrow nurses from the central pool of the hospital and must therefore give them the same conditions of work as in other wards. Nurses cannot be expected to do more than their statutory hours of duty and the idea of their living in with the patients is unthinkable. Yet this would be a distinct advantage and would help to reduce the impersonal atmosphere created by the shift system and the succession of adult figures that this involves throughout the day. According to hospital practice there are two sets of nurses who are alternately on duty. This involves having two charge nurses, a not altogether satisfactory ménage since it causes splitting of authority and provokes various reactions in our patients who are apt to make unfavourable comparisons or play up one charge nurse against the other.

In conclusion I should like to say that for anyone involved in the residential treatment of adolescents, the pressures and demands one must meet in the ward soon become, as Cameron said, "a test of personality". Adolescents quickly put you on your mettle, and greater endurance and emotional maturity are needed than in dealing with other age-groups. As one often hears: "It is bad enough to put up with one's children, who on earth wants to put up with other people's children?" And yet tolerance must govern our approach, there is no place for vindictiveness or regimentation if we are to prove ourselves worthy of our mission, which is to help the disturbed adolescent so often misjudged and misunderstood in our society.

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URBAN AND RURAL SUICIDE

By

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THE frequency of suicide differs between communities, countries, and historical periods. Though, in individuals, personal crises and peculiarities of personality structure are important in the causation of suicide, the differences in frequency referred to above are related to differing religious and social attitudes toward suicide and particularly to the degree of the individual's integration into a stable social group. This last influence, it has been suggested, is chiefly responsible for the difference between the suicidal tendencies of urban and rural areas.

It has long been known that usually suicide is proportionately more frequent in towns than in the country, and that this is so in many parts of the world (Durkheim, 1897; Sainsbury, 1955). In the literature which has been written on this aspect of suicide, however, the criterion of what constitutes an urban or a rural community appears to have been a purely administrative one. For example, the County Reports of the 1951 census in Great Britain sometimes include, among urban districts, communities of 1,000–2,000 persons, and among rural districts communities of 2,000–3,000 persons. This classification is unsatisfactory and distorts comparisons of urban and rural suicides based upon it.

It is therefore thought that closer attention might profitably be given to the differences between urban and rural suicides by abandoning the administrative classification in favour of one which gives a truer picture of the kinds of community in which the suicides had lived. For this purpose the word urban is here used to denote communities of 1,000 or more persons while communities of fewer than 1,000 persons are considered to be rural.

From the coroners' records of the suicides which occurred throughout Wales in the five years 1951–1955 information was extracted regarding the sex, address, occupation, and time of death, and this information is presented here against the suicides' setting in an urban or rural environment. The tables which follow show only crude rates, for standardized rates cannot be calculated since the ages of the county populations are known only for the Registrar General's designation of urban and rural areas. It is believed that any resulting inaccuracy of the comparative picture is only slight and is more than compensated by a more truthful and descriptive representation of the kind of community indicated by the words urban and rural.

URBAN AND RURAL SUICIDE RATES IN THE WELSH COUNTIES

Among the 2,173,560 inhabitants of the twelve Welsh counties (1951 census, excluding Monmouthshire), there occurred 881 suicides during the five years 1951–1955, an average annual suicide rate of 8.11 per 100,000 population. The urban suicide rate was 9.84 and the rural suicide rate 4.75.

These figures conceal great variations in the frequency of both urban and rural suicide between the counties, as Table I shows:

TABLE I

Average Annual Suicide Rates Per 100,000 of Population for Urban and Rural Areas of the Welsh Counties, 1951-1955

	Urban Rates			Rural Rates		
	Males	Females	Persons	Males	Females	Persons
Anglesey	10.96	1.93	6.16	12.99	1.27	7.06
Brecknockshire ..	21.35	9.66	15.55	10.91	5.1	8.05
Caernarvonshire	11.92	4.06	7.57	8.59	0	4.16
Cardiganshire ..	45.26	14.85	28.35	11.42	3.18	7.15
Carmarthenshire	17.7	9.19	13.24	10.0	4.31	7.12
Denbighshire ..	20.09	6.57	12.76	5.23	2.15	3.68
Flintshire ..	13.76	10.46	12.00	5.31	1.66	3.53
Glamorganshire ..	11.69	6.29	8.92	2.55	1.0	1.78
Merionethshire ..	21.52	8.62	14.74	11.13	1.79	6.71
Montgomeryshire	14.02	6.39	9.99	11.16	2.93	7.15
Pembrokeshire ..	12.11	7.99	10.0	11.86	3.42	7.66
Radnorshire ..	19.97	11.99	15.77	11.26	3.05	7.32

Urban suicide rates ranged from 28.35 per 100,000 population in Cardiganshire to 6.16 in Anglesey, and rural rates from 8.05 in Brecknockshire to 1.78 in Glamorganshire. In all counties with one exception, Anglesey, the urban suicide rate was higher for both sexes than was the rural rate.

The greater frequency of urban suicide may be explained by differences in the attitudes and social organization of urban and rural communities. In the country people are part of an ordered integrated society; they are knit into a stable parochial life and social relationships are firmer than in the towns. The need to conform and the benefits of conformity are greater. Those who live in the country tend to be satisfied with the interests available to them while those who are dissatisfied drift into the towns.

Though the social organization of rural life is usually defence against suicide, local conditions have been known to modify this. Dublin and Bunzel (1933) reported that in the Irish Free State from 1923 to 1928 the rural suicide rate was about 10 per cent. higher than the urban suicide rate. Schroeder and Beegle (1956) found that in Michigan the male suicide rate was higher in the country than in the towns while the female suicide rate was nearly equal in the two kinds of community. It was suggested that the usual urban : rural proportions of suicide were reversed in Michigan because many of the country dwellers had little part in the rural life; two-thirds of them were "fringe dwellers" working in urban occupations and having urban attitudes and tastes.

Without access to sociological data it cannot be known whether the reversal of the usual urban : rural proportions of suicides which was found among males in Anglesey is accountable in the same way, whether a conflict of urban and rural values and the disruptive influence, upon a hitherto insular community, of growing industry and commerce were responsible in this county for the highest rural male suicide rate in Wales. Certainly Glamorganshire, whose rural areas enjoyed the lowest male and the second lowest female suicide rate of any community in any county in Wales, showed no evidence that close proximity to industry and to densely populated urban areas has an adverse

effect upon rural suicide. The comparison is not, however, a proper one, for in Glamorganshire the rural areas have experienced during the last century or more a gradual development of industrialism in their midst, while in Anglesey the impact of urban standards and ways of living has been more immediate.

Before continuing this examination of urban and rural suicides a digression will be made to comment briefly on the differences which Table I shows between the suicidal propensities of the different counties and of the sexes. Suicide rates differ between countries and between different districts of a single city (Cavan, 1928; Sainsbury, 1955). It is therefore no matter for surprise that they should differ also between the counties in Wales. What is, however, remarkable is the great range through which the rates vary in this small country. These differences in suicide rates are not explicable by differences in the age composition of the county populations, for they remain much the same when the rates are standardized. It is outside the scope of this paper to discuss the significance of this. One might conjecture, on the basis of Sainsbury's work, why these differences exist between the counties, but the question which they pose deserves detailed correlation of medical and sociological data for contrasting counties, not merely with the aim of reducing the number of suicides, but to assess and reduce the degree of mental ill health which high suicides rates imply.

The preponderance of the number of male over the number of female suicides in every county in Wales agrees with that found in England and Wales as a whole (Stengel, 1952), but the wide difference between the suicide rates of the sexes in, for example, Anglesey (urban rates=10.96 male : 1.93 female; rural rates=12.99 male : 1.27 female) emphasizes the question why this difference between the sexes should exist. As long ago as 1897 Durkheim called suicide "an essentially masculine phenomenon". The male suicide rate is known to be more variable in response to stresses than is the female suicide rate (Sainsbury, 1955) and may reflect social conditions against whose effects women are more protected by the more circumscribed domestic functions which they perform. The difference between such counties as Anglesey and Flintshire in their male : female suicide ratio suggests a need for sociological research to test this hypothesis and to identify those conditions which foster or discourage suicidal tendencies in one sex more than in the other.

THE SIZE OF THE COMMUNITY AND SUICIDE

The line of demarcation between rural and urban communities adopted in this study (a population of 1,000 persons) marks also the division between a suicide rate of 4.75 per 100,000 and one of 9.84. It is clearly unlikely that this enormous increase in suicidal tendency should occur precisely at this population level. The question then forces itself on one's attention whether the general rural and urban rates conceal an increasing suicidal trend in progressively larger communities. There are degrees of urbanization and rurality, and direct relationships have been found elsewhere between the degree of urbanization and frequency of suicide. Suicide rates in the U.S.A. are higher in the larger towns than in the smaller (Henry and Short, 1957; Dublin and Bunzel, 1933; Cavan, 1928).

Similar results were not, however, found among the towns in this present study, consequently numbers of suicides are not given here for sizes of towns. One interesting fact which did emerge was that the change of suicide rate was very marked at about the 1,000 of population level. The rural suicide rate was 4.75 while for towns whose population was 1,000-2,000 persons the rate was

8.53. It was not possible to calculate suicide rates for different communities of smaller sizes than 1,000 persons, for the sizes of the rural communities in which suicides occurred were indefinite. The address of a rural suicide, recorded at the inquest, was merely the postal address and might have related the suicide to the nearest hamlet though he lived alone a mile away.

Suicide and Density of Population

Though rural suicides could not always be placed in communities of definite sizes, as urban suicides could be, a crude measure of the degree of physical contiguity in country districts is given by the densities of population per acre recorded by the County Census Reports of 1951, and the rural suicide rates of the counties may be compared with these. Suicide rates for the rural areas of the different counties are shown with the densities of population in Table II.

TABLE II

Average Annual Rural Suicide Rates Per 100,000 Population, and Density of Population, the Welsh Counties, 1951-1955

	Rural Suicide Rates			Persons Per Acre in Rural Districts
	Males	Females	Persons	
Anglesey	12.99	1.27	7.06	0.2
Brecknockshire	10.91	5.10	8.05	0.1
Caernarvonshire	8.59	0	4.16	0.2
Cardiganshire	11.42	3.18	7.15	0.1
Cararthenshire	10.00	4.31	7.12	0.2
Denbighshire	5.23	2.15	3.68	0.2
Flintshire	5.31	1.66	3.53	0.5
Glamorganshire	2.55	1.0	1.78	0.7
Merionethshire	11.13	1.79	6.71	0.1
Montgomeryshire	11.16	2.93	7.15	0.1
Pembrokeshire	11.86	3.42	7.66	0.1
Radnorshire	11.26	3.05	7.32	0.05

This Table shows that the counties with the most sparsely populated rural areas tended to have the highest rural suicide rates. Thus, six counties with a rural population of not more than 0.1 persons per acre all had rural suicide rates of more than 6 per 100,000, while the two counties with the most densely populated rural areas (Flintshire and Glamorganshire) had rural suicide rates of only 3.53 and 1.78. There was a high negative correlation between rural male suicide rates and density of rural population ($r = -0.83$).

The relationship between density of rural population and the rural suicide rates of the two sexes is illustrated in the histogram (Fig. 1).

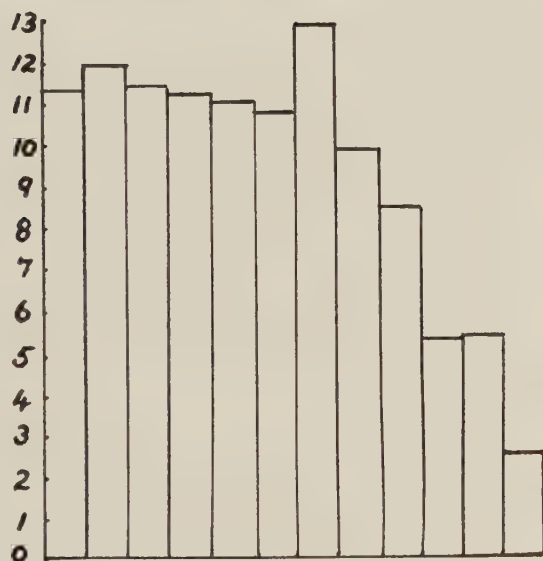
There appears to be a general though irregular tendency towards an association between female suicide rates and density of population, while the rural male suicide rates show an almost constant decline with increasing density of rural population in all counties except Anglesey. It will be remembered that this county had another peculiarity: it was the only county whose rural suicide rate exceeded its urban rate.

What the reason may be for this relationship between rural suicide rates and density of rural population it is possible only to speculate at present. In isolated communities the paucity of social contacts may be responsible for higher suicide rates, or there may be some other influence such as comparatively unprofitable farming land which may cause both sparsity of population and a

Persons per acre
in rural districts,
by counties shown
in rank order



Suicide rate
per 100,000
males in
rural districts,
by counties



Suicide rate
per 100,000
females in
rural districts,
by counties

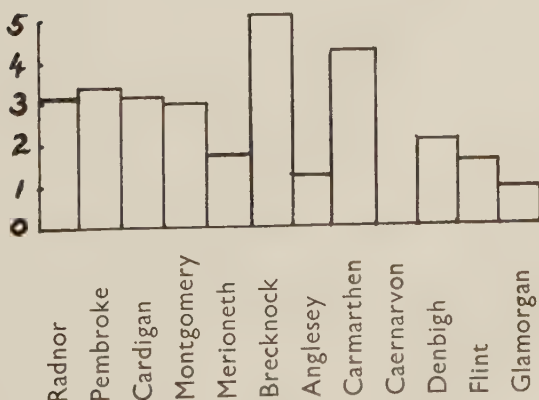


FIG. 1

more precarious livelihood, and consequent greater hardship and stress. Whatever the cause may be, women are apparently less affected by it than are men. As Sainsbury (1955) has remarked, women have a certain immunity to stresses

by virtue of their more ordered role within a domestic setting, while men are required to play a more aggressive individualistic role and are more exposed to stresses outside the home.

Suicide Among Farmers

The impossibility of relating rural suicides with certainty to hamlets or villages of identifiable size has been mentioned, but even though the number of suicides in intermediate sized rural communities is not known it is possible to determine the number in more extreme rural isolation. Farms are physically separate from other dwellings and often their isolation is considerable or extreme.

There were approximately 32,000 farmers in the twelve counties. (An estimate provided by the Welsh Department of the Ministry of Agriculture, Fisheries and Food. The Occupation Tables of the 1951 census give only the number of farmers and farm foremen combined.) In the five years of this study, there occurred 46 suicides among farmers; their suicide rate was 28.7 per 100,000. This rate is higher than that for any other group of persons, male or female, urban or rural, with the exception of the urban males in Cardiganshire. It is more than twice as high as the rural male suicide rate in any county.

It would appear then that the observation made above regarding sparsity of rural population and high suicide rates is supported by the frequency of suicide among farmers, but some consideration should first be given to possible influences other than isolation, namely age and specific stresses associated with the occupation of farming.

In comparing suicide among farmers with suicide among the remainder of the rural male population the balance of age is weighted against the farmers since the general rural male population includes children and young persons among whom suicide is comparatively rare, while it might be supposed that farmers would include many of the older and more vulnerable age groups. Suicides among farmers, however, tended to be younger than other rural male suicides; 78 per cent. of farmer suicides were below the age of sixty, while 57 per cent. of the other rural male suicides were below that age.

The influence of possible stresses peculiar to farming is less easily assessed. The "reasons" for suicide, even when given by attempted suicides who survive to be questioned, shed only a dubious light on the problem and are less reliable still when they are merely the opinion of relatives or friends who may have reasons, conscious or unconscious, for concealing or distorting the truth. In any case the expressed motives give only an incomplete explanation and are merely rationalizations of underlying emotional difficulties. The evidence given regarding the motives of these 46 farmer suicides was no more enlightening than for other suicides. Three appeared to have been psychotic, with paranoid delusions. Five were worried about physical ill-health. Six were worried about financial or labour difficulties in the farm. Fifteen had been depressed for some months for no known reason. Five were said to have appeared normal, well, and unworried. For the remainder a variety of reasons was given: bereavement, changed domestic circumstances, shame and fear of exposure. Involutional depression may be precipitated by environmental influences. Physical disability of recent sudden onset may cause feelings of helplessness and of despair regarding the future. Possibly the anxieties of this nature may be keener in farming, but otherwise there is no indication of stresses peculiar to this occupation.

It has been shown that rural male suicides are most common in the counties whose rural areas are least populous. It appears probable that the high suicide rate among farmers is an extension of this tendency and is related to their isolation.

Suicide and Isolation

We are gregarious beings. Social isolation, said Sainsbury (1955), explains the high suicide rate in certain London boroughs. There is a high suicide rate among immigrants who have not yet become incorporated into the community in a strange country (Strauss, 1956).

The conditions which constitute social isolation cannot be specified simply. The number of people in a person's environment is no indication of the number of his social attachments. A sense of isolation may be present without actual physical isolation as in "subjective excommunication" (Strauss, 1956) when the individual feels himself excluded from society on account of old age or loss of social status. Residence in a crowded town is no security against loneliness, and life in a small country hamlet does not necessarily signify isolation. Nevertheless the smaller the community the fewer the possible social contacts, and in remote farms the social bonds may be very few.

It cannot be said that farmers are isolated in the sense that transient dwellers in boarding houses are isolated, but inquest records show evidence that holdings which some suicides farmed were poor and employed perhaps one or two labourers. A farmer on such a holding must spend much of his time in solitude. The number of suicides which occurred on such farms is unknown, but the writer was told by two coroners for predominantly rural areas that they had observed that an appreciable number of suicides occurred in the most isolated parts of their districts.

The effects of physical isolation have been the subject of biographical and experimental studies. The experiences of persons who survived partial or complete isolation at sea or in polar conditions showed a similarity in their mental reactions. Psychotic manifestations were almost invariable among those who survived singly and were experienced also, though less often, by those who survived in small groups (Raines, 1956).

Frost (1938) said that mechanisms released by solitude include hallucinatory projection so that suicide may occur at the command of hallucinatory voices. Physical isolation can produce effects similar to those of any other stress and may so magnify any coincident stresses that mental symptoms appear more intensely (Lilly, 1956). In isolation from external stimulation one is thrown more on internal resources (Bruner, 1959).

These studies may indicate the nature of the morbid state which underlies the proneness of farmers to suicide, and they support the suggestion made above that physical isolation may be responsible for the relatively high suicide rates which were found in the most sparsely populated rural districts.

SEASONAL VARIATIONS OF SUICIDE IN TOWN AND COUNTRY

Morselli (1881) observed that suicide was commoner in spring and early summer than in other seasons, and this observation has been repeated by various writers (Durkheim, 1897; Dublin and Bunzel, 1933; Dahlgren, 1945; Swinscow, 1951). The monthly distribution of the suicides throughout Wales substantially agreed with this. The highest peak occurred in the spring. A lesser peak occurred in the autumn. July and August showed a low elevation which

was apparent also in the graphs provided by Swinscow (1951) for England and Wales.

It is known that the variations in suicidal frequency are associated with the seasons and not with the months of the year, for Swinscow pointed out that the converse monthly distribution of suicides occurred in Australia. Since this is so it was thought that it might be profitable to examine the seasonal behaviour of suicidal trends in rural communities where the cycle of the seasons has its greatest impact and significance. The following graphs show the monthly standardized figures expressed as a percentage of the five years' total of suicides. (Crude figures for the monthly incidence of suicide are standardized to compensate for the different lengths of the months.)



FIG. 2.—Monthly distribution of suicides, Wales. 1951–1955.

The graphs show that though there are resemblances between the seasonal fluctuations of urban and of rural suicides the amplitude of the fluctuations is greater in the country than in the towns. The rural range is from 5 per cent. to 12.3 per cent. while the urban range is only from 6.8 per cent. to 9.9 per cent.

The reason for the seasonal variations in the frequency of suicide is not known. Morselli (1881) suggested that the unaccustomed warmth of spring caused "irritability". Fifty years later, Mills (1935) said that the weather was more influential than economic conditions in the determination of suicide rates, and that suicide was most common in districts where changes in temperature and barometric pressure were severe and common. Durkheim (1897)

believed that the explanation was to be found in the reduction of social integration by the migration of labour to the countryside in early summer, and in the lengthening period of daylight. Certainly suicide more commonly occurs in the hours of daylight, but the days are longer in June than in April while suicide is less frequent in the former than in the latter month, and it is doubted whether the migration of labour is today as extensive as it was when Durkheim wrote. More recently it has been observed that admissions to mental hospitals have a similar seasonal distribution, and that this may indicate that for some unknown reason the relationship between the individual and his environment is more strained in the warmer than in the cooler months (Swinscow, 1951).

There were no definite indications among the present findings to show why the number of suicides fluctuates in the seasons of the year. A certain peculiarity was, however, remarked which shows a possible method of approach to this problem.

It might be anticipated that seasonal variations in frequency would be more pronounced among rural than among urban suicides, for life is regulated more by the seasons in the country than it is in the towns, but we have seen that there occurred in addition in rural areas a high summer peak of suicides which was greater than the usually reported spring and autumn peaks. Probably this fact emerged because the criterion of rurality applied here was more definite and restrictive than the administrative classification upon which statistics are usually based.

This is a matter which deserves further attention for if, as is generally thought, some coincidental social change causes the seasonal variations in the number of suicides, then the observation, in this study, of a great and almost exclusively rural increase in suicide in mid-summer indicates a defined and limited problem whose solution might give an answer to the larger problem. The social change to be investigated would be annually recurrent, confined to mid-summer, and restricted to rural areas. The result of such investigation would not merely be of value for the prevention of suicide, but might indicate measures of value to mental health in general.

SUMMARY

In Wales, as commonly occurs in other countries, suicide was proportionately more frequent in towns than in the country. This was so in nearly every county and in both sexes. Rural suicide rates for females were particularly low.

A remarkable increase in the suicide rate occurred between communities of under 1,000 persons and those of 1,000–2,000, but there was no constant increase in the frequency of suicide in progressively bigger towns such as has been described elsewhere. Neither was there apparently a continued fall of suicide rates in progressively smaller communities in rural areas. On the contrary, though it was not possible always to relate a rural suicide to a community of known size, there were indications that suicide became more common, particularly among men, as rural communities became smaller and more scattered. There was a high negative correlation between suicide rates of males in rural areas and the density of rural population.

The vulnerability to suicide shown by males in sparsely populated rural areas was particularly marked among farmers whose conditions of living and working must necessarily be more isolated than those of other country dwellers. The results of experimental and other investigations into the effects of physical

isolation suggest a possible explanation for the relationship between sparsity of population and high rural suicide rates, and for the frequency of suicide among farmers.

Seasonal variations in the frequency of suicide in the total population followed the usually reported pattern of vernal and autumnal increases. In the country, however, these variations were much more pronounced than they were in the towns. A mid-summer increase in the number of rural suicides was particularly prominent and offers a suitable limited problem for further examination.

Two incidental findings suggest topics for research: (1) the substantial differences between the counties in their proneness to suicide; (2) the varying degrees among the counties by which female suicide rates differed from male suicide rates.

ACKNOWLEDGMENTS

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THE DESCRIPTION AND INTERPRETATION OF PICTURES IN CASES OF BRAIN LESION

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INTRODUCTION

PICTURE material may be "described" or "interpreted". This distinction (further discussed in the section on Analysis of Results) is related in part to the complexity of the material, in part to the kind of response that is required. Defective description of pictures in cases of brain lesion has aroused little comment and has not been claimed to exist as an isolated disability. In contrast impaired interpretation of picture material has been more frequently found in association with disease or injury of the cerebral hemispheres. Moreover there is little agreement concerning the nature of this disability.

Some authors have considered it to be a circumscribed visual disorder. Thus Poppelreuter (1917, p. 184) in his study of cases of occipital injury, and Hoppe (1921) in his careful clinical report of one case have described primary disturbances of the ability to understand the meaning of pictures. In other cases the defective interpretation of pictures has been manifested in association with, and probably as a consequence of, other forms of visual disorder—with unilateral visual neglect (Scheller and Seidemann, 1931), or with defective visual-spatial analysis (Duensing, 1954). In yet a third form of the disability, a defect in the synthetic activity by which details are related to each other to give the meaning of the whole has been suggested as the basis of the impairment of picture interpretation. This form of the disorder was termed "Simultanagnosie" by Wolpert (1924) and "semantic aphasia" by Head (1926). The defect of synthesis might extend beyond purely visual perception in the opinion of both of these authors, but was not similar to general intellectual deterioration. Critchley (1953, p. 373) has likewise referred to faulty interpretation of pictures in mild cases of aphasia lacking all other evidence of visual disturbance. Finally some authors have reported cases in which non-selective intellectual deterioration combined with a circumscribed lesion in the occipito-parietal areas was thought to give rise to the disordered interpretation of pictures (Lange, 1936).

It is the purpose of the present paper to present results on a quantitative test of picture description and interpretation for a group of 30 neurological patients. In order to achieve quantification it proved necessary progressively to increase the brightness of the material; so that the final measure of performance reflects the subject's ability to give a correct description or interpretation within certain limits of brightness and duration of presentation of the material.

METHODS

Subjects. A control group was formed of 48 subjects, drawn from the hospital staff. As far as is known no member of this group was suffering from

neurological or other disease. The range of ages was from 17-61 years, with a mean of 33·8 years. Details of age, sex and occupation for each member of this group are to be found elsewhere (Ettlinger, 1955).

Two groups of neurological cases were studied. The first group consists of 26 cases in which the nature and location of the lesion is known. This informa-

TABLE I

Details of Diagnosis, Age and of Performance at Picture Description and Interpretation in Neurological Cases with Known Site of Lesion

Hospital No.	Diagnosis or Site of Lesion	Age	Field Defect	Perceptual Disorder	Score at	
					Picture Description	Picture Interpretation
57776	L. front. angioma (verified by arter.)	42	—	—	118	71
49695	L. fronto-temp. glioma (verified at op. and histol.)	27	—	—	59	39
57682	L. parasag. fronto-par. G.S.W. (verified at op.)	57	—	—	95	47
36314	Excision L. parasag. fronto-par. glioma	37	—	—	94	41
57928 (left-handed)	R. mid-fronto-par. G.S.W. (verified at op.)	35	—	—	245	95
57818	R. mid-fronto-par. G.S.W.	30	Low l.h. quadranopia	—	71	55
14139	R. front. scar (aspir. of abscess) (verified at op.)	15	—	—	90	59
51589	Bil. front. glioma (verified at autopsy)	30	—	—	45	51
57245	Glioma of corp. call. in fronto-par. region (verified at op. and histol.)	38	—	—	73	59
16981	Excision spiking focus from L. temp. lobe	19	—	—	57	44
46777 (aphasic)	L. temp. haematoma (verified at op.)	23	—	—	94	59
57490 (aphasic)	Evac. L. temp.-par. subdural haematoma	33	—	—	137	74
18840	R. temp. lobectomy	18	Up. l.h. quadranopia	—	50	45
56664	R. temp. lobectomy	31	—	—	81	45
2288	R. temp. lobectomy	30	Partl. l.h. hemian.	—	124	81
44633 (left-handed)	R. temp. glioma (verified at op. and histol.)	56	—	—	100	82
45798	L. par.occip. infarct (verified at op.)	45	R.h. hemian.	Impd. picture interpretation	74	51
53718	Aspir. R. par. glioma (verified histol.)	49	L.h. attent. hemian.	Visual-spatial agnosia	104	88
55605	R. par. angioma (verified by arter.)	61	L.h. hemian.	Visual-spatial agnosia	151	103
56534	R. par.-occip. glioma (verified at op. and histol.)	51	Partl. L.h. hemian.	Visual-spatial agnosia	94	78
57486	Shrunken gyri in R. par.-occip. region (verified at op.)	13	Constriction of L.h. fields	—	87	45
54117	R. par.-occip. mening. (verified at op.)	43	L.h. hemian.	—	115	52
57925	L. > R. parasag. par. G.S.W. (verified at op.)	45	—	—	136	79
56413	R. extra-occip. mening. (verified at op.)	49	Constriction of L.h. fields	Impd. picture descr. and interp.	172	48
53059	R. occip.-temp. second. deposits (verified at autopsy)	57	L.h. hemian.	Visual-spatial agnosia	180	76
55182	L. > R. parasag. occip.-par. G.S.W. (verified at op.)	27	Partl. R.h. hemian.	—	90	49

tion became available as a result of surgical intervention, *post mortem* examination or arteriography. Details of the cases in this group are given in Table I. The mean age for these 26 patients is 36.9 years, with a range from 13-61 years.

A further group of patients diagnosed as suffering from neurological disease and thought likely to have circumscribed lesions was studied. The precise location of the lesions could not, however, be verified in any of these cases. Nevertheless 12 of these cases have been used for certain comparisons where the location of the lesion need not be known. The 12 were selected from the larger group because each of these patients had been examined on tests of visual sensory efficiency which have been previously described (Ettlinger, 1956). Details of the cases in this group are given in Table II. It should be noted that the cerebral hemispheres were probably not involved in three of these cases (cases of optic atrophy).

TABLE II

Details of Diagnosis, Age and of Performance at Picture Description and Interpretation in Neurological Cases with Unknown Site or Extent of Lesion

Hospital No.	Diagnosis or Findings	Age	Field Defect	Perceptual Disorder	Score at	
					Picture Description	Picture Interpretation
57295 (left-handed)	R. hemiparesis	38	—	—	80	75
31816	Focal ep. R. front. EEG focus	45	—	—	97	44
56904 (aphasic)	Ep. L. temp. EEG focus ..	52	—	—	87	44
48257	Ep. of unknown aetiology ..	26	Variable	—	163	88
55795 (aphasic)	Cortical atrophy (verified by AEG)	53	Low L. + R. defect in L. eye	Impd. picture interp.; mild visual-spatial disorder	158	87
53222	Basilar artery occlusion ..	63	R.h. hemian.	Visual alexia	133	101
59317	Bil. occip. infarcts	52	Up. L. + R. h. defects	Prosopagnosia	163	98
53120 (aphasic)	L. occip.-par. second deposits	53	R.h. hemian.	Visuo-construct. disorder	161	88
58227 (left-handed)	Mid-brain damage from closed H.I.	22	—	—	163	82
57690	Failure of vision; suprasellar mening.	27	Bi-temporal constriction	—	120	51
57043	Optic atrophy; pituitary adenoma	61	Extensive field defects	—	113	78
51484	Optic atrophy; demyelin. disease	34	Extensive field defects	—	186	78

Apparatus. A modified version of the "dazzle-tachistoscope" designed by G. C. Grindley was used. This apparatus is illustrated in Figure 1. When the subject looks through the eye-piece (with one eye) he can always see the background by reflection in the glass screen set at 45 degrees to his line of vision. The background consists of light grey dots spaced irregularly on a darker grey ground. The amount of light incident upon a picture placed into the picture holder is controlled by a variable neutral density filter. The transmission of the filter is linearly related to the rotation of a shaft which is driven by a constant-speed electric motor. A pointer on the shaft traverses a dial marked off in 42 equal divisions and adjusted so that a black-white picture is invisible at zero and plainly visible at 42.

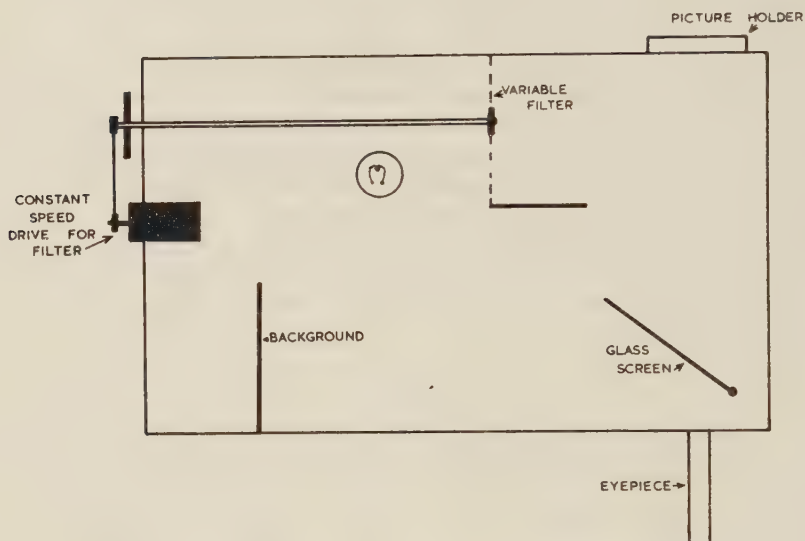
DAZZLE TACHISTOSCOPE

FIG. 1.—Plan of apparatus (which is fully described in the text).

The apparatus is used in a screened room in which the only light source is a 100-watt bulb at 3 metres above the apparatus. The overall luminance of the ground of the pictures is 0.2 foot L. when the pointer reads zero and 1.0 foot L. at 42 divisions. The motor moves the pointer from zero to maximum in 60 seconds. The eye-piece restricts vision to a circular area subtending 10.5 degrees at 46 cm.

With this apparatus, any reading on the dial above zero reflects two variables: first, an increase in luminance of the picture, and secondly, an increase in the duration of exposure of the picture (since some outlines become visible at readings only a little above zero).

Material. A standard series of 30 pictures is used for all subjects. This material falls into 6 groups (A–F) of 5 cards. The first group (simple designs) is used for practice only. Group B contains simple black outline shapes such as a diamond; group C silhouettes of shapes or objects in black on white such as an arrow-head; group D similar silhouettes, but of more complex objects and figures such as a yacht; group E outline pictures of events and actions such as a policeman leading two children across a road; group F complex silhouettes in white on black such as a guardsman.

Procedure. The eye with the larger intact field as measured perimetrically is used. When there is no difference between the eyes selection is made by a random procedure. The 30 pictures are always presented in the same order during one session lasting about half an hour. The subject is told that this is a test of brightness discrimination and that pictures, at first too dim to be seen against the background, will begin to appear at any time after a warning. He is asked to respond to two conditions for each picture: first, as soon as he can distinguish any shadow forming against the ground (that is, before he knows the content); and again as soon as he can identify the content. He is urged to guess as soon as

possible at the content, and to report as much about it as he can. He is informed if he makes a mistake, but no other help is provided except that certain standard questions are asked if a correct identification but inadequate interpretation has been given (as for example, when, following the response, "A figure of a man", for a picture of a praying monk, he is asked, "What is his profession?"). Each subject is allowed a further period of 60 seconds if no correct answer is forthcoming by the time that the pointer has reached 42. Answers correct during this interval are scored 43, otherwise the subject is said to have failed on that card. Evidence is presented elsewhere (Ettlinger, 1955) that performance by control subjects under these conditions is largely limited by the brightness of the material rather than by the rate of increase in brightness.

Analysis of results. Certain of the 30 cards were considered to require description, others interpretation. This distinction is based upon both the complexity of the particular picture and on the nature of the answer that is scored as correct. It is related to the similar distinction made by Terman and Merrill (1937, p. 336). Description includes their category of enumeration. For interpretation, "the subject must bring the elements of the picture together . . .". The allocation of the 30 cards into two categories was made before the results were analysed.

Each subject was assigned one "final" numerical score on each card, so that certain of these scores relate to proficiency at picture description, others at picture interpretation. A detailed account and validation of the method of deriving the final scores may be found elsewhere (Ettlinger, 1955). In summary, the final score for a given card is the mathematical difference between the value of the pointer at the time of correct description (or interpretation) and the value of the pointer at the time of the first appearance of a shadow forming against the ground.

It was found that the final scores of the 48 control subjects ranged between zero and 35, with the additional category of failure (now scored as 36). All cards on which more than one control subject had failed were next excluded from further analysis (so that failure by patients would not be likely to result from below-average intelligence or refractive errors). There remained 10 cards thought to test picture description two of which are shown at the top of Figure 2. For each of these cards only the name of the representation was required. In addition there remained only three cards on which no more than one control subject had failed and which were thought to require interpretation. Two of these cards are shown in the lower part of Figure 2. For each of these three cards interpretations of the actions or of the events taking place were required.

Every patient was tested on the full series of 30 cards. However final scores were computed for only 13 cards. The sums of final scores respectively for description (10 cards) and interpretation (3 cards) are given for each patient in Tables I and II.

RESULTS

In Table III are shown the results of comparisons between performance by various groups of subjects at picture description and interpretation. In all comparisons of the difference between mean scores the non-parametric test devised by Mann and Whitney (1947) has been used. The p columns in Table III give the one-tailed probability that the two groups of subjects in each comparison have been drawn from the same population.



FIG. 2.—Samples of picture material. The yacht and telephone box are examples of cards requiring description. The running child and policeman leading children across the road are examples of cards requiring interpretation.

It is seen from the first comparison of Table III that the scores of 26 cases with known cerebral lesions are raised (indicating poor performance) both at picture description and interpretation relative to those of the control subjects. This difference attains statistical significance so that the presence of a cerebral lesion is seen to impair both the description and interpretation of pictures.

While there is no significant difference between cases with unilateral and bilateral lesions (second comparison) it is seen from the third comparison that cases with right-sided lesions are significantly impaired relative to those with left-sided lesions at picture interpretation but not at description of pictures. Since there were field defects in 10 of the 14 cases with right-sided lesions (but only in one of the eight with left-sided lesions) a further comparison between cases with left- and right-sided lesions was made after excluding all cases with field defects. This fourth comparison (involving only 11 subjects) fails to reach significance. However the trend towards a higher mean score (worse performance) at picture interpretation for right-sided cases is still marked. The

TABLE III

Mean Scores at Picture Description and Interpretation in Various Groups of Subjects and Results of Statistical Analyses

				Picture Description		Picture Interpretation	
Subjects		n	Mean Score	p	Mean Score	p	
1. Control subjects ..	..	48	68·8		50·6		
Patients (Table I) ..	..	26	105·2	0·0002*	62·2	0·0022*	
2. Unilateral lesions ..	..	22	108·7		62·6		
Bilateral lesions ..	..	4	86·0	0·1271	59·5	0·5000	
3. Left-sided lesions ..	..	8	91·0		53·3		
Right-sided lesions ..	..	14	108·9	0·1379	68·0	0·0260*	
4. Lefts (no field defect) ..	..	7			53·6		
Rights (no field defect) ..	..	4			70·3	0·1830	
5. R. frontal lesions ..	..	3			69·7		
R. non-frontal lesions ..	..	11			67·6	0·2912	
6. R. temporal lesions ..	..	5			65·8		
R. non-temporal lesions ..	..	9			69·2	0·2743	
7. R. parieto-occipital lesions ..	..	9			71·1		
R. non-parieto-occipital lesions ..	..	5			62·4	0·2327	
8. Frontal lesions ..	..	9	98·9		57·4		
Non-frontal lesions ..	..	17	108·6	0·2676	64·7	0·1949	
9. Temporal lesions ..	..	9	98·0		60·6		
Non-temporal lesions ..	..	17	109·1	0·3228	63·0	0·2843	
10. Parieto-occipital lesions ..	..	16	119·9		65·0		
Non-parieto-occipital lesions ..	..	10	81·8	0·0212*	57·6	0·1635	
11. Parieto-occipital lesions (no aphasia) ..	..	15	118·7				
Non-parieto-occipital lesions (no aphasia) ..	..	9	80·4	0·0281*			
12. Parieto-occipital lesions (field defect) ..	..	10	118·5		65·5		
Non-parieto-occipital lesions (field defect) ..	..	5	118·6	0·0708	66·6	0·2643	
13. Parieto-occipital lesions (no field defect) ..	..	6	130·0		80·5		
Non-parieto-occipital lesions (no field defect) ..	..	8	65·8	0·0410*	56·3	0·2070	
14. Aphasic ..	..	5	127·4		73·6		
Non-aphasic ..	..	33	112·8	0·2327	66·2	0·3015	
15. Field defect ..	..	20	125·5		72·0		
No field defect ..	..	18	102·8	0·0268*	60·6	0·0188*	
16. Control subjects ..	..	48	68·8		50·6		
No field defect ..	..	18	102·8	0·0060*	60·6	0·0094*	

In the column headed n are given the number of subjects in each group. In the column headed p are given the probabilities of the two groups in each comparison being drawn from the same population, that is, of no difference between the groups. The symbol * indicates a significant difference between the groups in any comparison.

fifth to seventh comparisons involve only the 14 cases with right-sided lesions (irrespective of the presence of field-defects), and indicate that the location of the lesion within the right hemisphere is not an important determinant of impairment at picture interpretation.

For comparisons 8-10, cases with left- and right-sided lesions have been combined with cases having bilateral lesions in order to ascertain whether the location of the lesions respectively in the frontal, temporal or parieto-occipital areas is an important determinant of impairment at picture description or interpretation. Patients have been assigned to a given lesion group if there is any evidence of the lesion extending into that area. For example, a case of fronto-parietal G.S.W. (with predominant injury to the frontal region) has been included not only in the frontal group, but also in the parieto-occipital group. Such a case would also belong to the non-temporal group, but *not* to the non-frontal or non-parieto-occipital groups. It was considered inadvisable to compare the effects of parietal and occipital lesions separately because there are only three cases with lesions situated predominantly in the occipital lobes. It is evident from comparisons 8-10 that the location of the lesions is not an important determinant of defective picture description or interpretation except in one instance: cases with parieto-occipital involvement are significantly impaired relative to cases with lesions elsewhere at picture description but not at picture interpretation (comparison 10). This difference remains significant (comparison 11) after all cases of aphasia have been excluded. However a further comparison between cases of parieto-occipital lesion with field defects, and cases without involvement of the parieto-occipital areas but having field defects (comparison 12) indicates that the latter group is more impaired. This group (that is cases without involvement of the parieto-occipital areas but having field defects) comprises three cases with field defects associated with optic atrophy (taken from the cases described in Table II) and two cases of temporal lobe lesion (Table I). This finding would suggest that the presence of a field defect is a more important determinant of impaired picture description than the location of the lesion in the parieto-occipital areas. Nevertheless the further comparison between cases with parieto-occipital involvement but without field defects, and cases without parieto-occipital involvement having no field defects (comparison 13) indicates that location of a lesion in the parieto-occipital areas is an important determinant of impairment at picture description even when the influence of field defects has been excluded.

In evaluating the effect of aphasia and impaired vision on picture description and interpretation the cases described in Tables I and II have been combined (since the location of the lesion is not of importance for these analyses). It is evident that the deterioration of picture description and interpretation associated with aphasia (comparison 14) fails to reach statistical significance. However the impaired description and interpretation associated with the presence of field defects (assessed perimetrically) is sufficient to distinguish between cases with and without field defects at a significant level of confidence (comparison 15). The final comparison of Table III indicates that the presence of field defects is not the only determinant of defective performance by neurological patients with picture material. For the group of 18 cases without field defects is still significantly inferior to the control group at both description and interpretation. This conclusion derives some measure of support from a further finding. Thus there is no significant correlation between visual sensory efficiency as assessed by the techniques described elsewhere (Ettlinger, 1956) and respectively performance at picture description and interpretation in 29 cases

(Spearman rho of -0.28 for description, -0.31 for interpretation; $p > 0.05$ in both cases).

Summary of results. The quantitative analysis indicates that cases with cerebral lesions are as a group impaired at picture description and interpretation (as measured by the present methods); that cases with right-sided lesions show a greater degree of impairment of *interpretation* than do cases with left-sided lesions; that cases with the lesion situated in the parieto-occipital areas are more severely impaired at *description* than are cases with lesions situated elsewhere (and this is not entirely due to the field defects associated with parieto-occipital lesions); and that cases with field defects are less proficient at both description and interpretation than cases without field defects (although the latter group is still impaired in comparison with the control group).

DISCUSSION

It is perhaps not surprising that patients with disease or injury of the cerebral hemispheres are impaired as a group on tests of picture description and interpretation. This result finds some confirmation in the report of Weinstein and Teuber (1956) who investigated performance on a test of figure-ground discrimination. However in their study a greater degree of impairment was selectively associated with dysphasia and not with the presence of field defects, whereas the reverse is true in the present investigation. The present findings appear to correspond more closely to those of Poppelreuter (1917), placing emphasis on a predominantly visual component in the disability, than to those of Head (1926), placing emphasis on a synthetic component related to language. However it must be recalled that only five subjects in the present group of 38 were dysphasic, and that a trend towards greater impairment in these five cases can be detected.

Further evidence for the dissociation between defective interpretation of pictures and dysphasia comes from the present finding of a greater degree of impairment in cases with right-sided lesions than with left-sided lesions. Milner (1958) has reported that patients with right temporal lobe lesions are more severely impaired on a test of visual intelligence (Picture Anomalies) than are patients with left temporal lobe lesions. The present test of picture interpretation was designed to evaluate mainly perceptual and not intellectual performance (if this distinction can be made) by excluding all cards from the final analysis on which more than one of 48 control subjects had failed. Moreover no one site of lesion within the right hemisphere was found to be a major determinant of impairment. Therefore the relationship between the present findings—of more impairment at picture interpretation in cases with right- than with left-sided lesions—and the results of Milner requires further clarification.

Nor is the selective effect of lesions situated in the parieto-occipital areas in giving rise to impaired description of pictures fully understood. This effect remained even after cases with dysphasia and field defects had been excluded from the analysis. It is noteworthy that the same cases are not significantly more impaired at picture interpretation than cases with lesions elsewhere. However the following explanation may be offered for this apparently paradoxical result. With the present methods of testing, the score on picture description, but not interpretation, is largely determined both in control subjects and patients by the subject's ability to distinguish areas of differing brightness. The cases of parieto-occipital lesion may have been impaired predominantly in this aspect (contour perception) of the picture description test. With picture interpretation,

however, even the control subjects gave scores indicating that the picture was clearly visible some time before a correct interpretation was given. Therefore interpretation is less intimately related in this test to the brightness of the picture than is description.

Finally it must be admitted that quantification has been achieved only at a cost: the present tests of picture description and interpretation may not be truly comparable with similar tests given clinically. For example the restriction of the field of exposure to $10\cdot5$ degrees of arc, the use of only one eye and the variation in the brightness of the material may have served to limit the generality of the present results. Some evidence for this is seen in the lack of correspondence between impairment as assessed clinically and as measured quantitatively (see Table I). Such discrepancies remain to be resolved by further studies.

SUMMARY

The performance of a group of 30 cases of brain lesion at describing and interpreting picture material has been measured quantitatively.

It is found that the group of patients as a whole is significantly impaired at both tasks relative to a control group of healthy subjects. However the presence of field defects gives rise to a significant added measure of difficulty at both description and interpretation of pictures, whereas the presence of aphasia does not. The site of lesion is found not to be an important determinant of deficit except that (1) cases of parieto-occipital lesion are significantly impaired at picture description, and (2) cases of right-sided lesion are significantly impaired at picture interpretation.

These findings are discussed and related to previous work.

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AN EVALUATION OF ELECTROPLEXY (E.C.T.) TECHNIQUES

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I INTRODUCTION AND PROBLEM

THE court hearing (*Bolam v. Friern Hospital Management Committee*) showed that British psychiatrists disagreed about the best technique of administering electroplexy. The implications of this were discussed in a recent communication (1), which also contained an extensive review of the literature showing a similar disagreement amongst previous authorities. In order to ascertain which E.C.T. techniques were most widely practised in this country, a questionnaire was circulated to a number of mental and teaching hospitals and the results of this, which were reported in full (1, 3), are summarized in Table I.

TABLE I

E.C.T. Techniques in Current Use in 48 British Hospitals in 1957
Male Patients

	No.	Percentage
E.C.T. modified with Pentothal and Scoline	29	60
E.C.T. modified with Pentothal and Brevidil "E"	7	15
E.C.T. modified with Brevidil "E" alone	4	8
E.C.T. modified with the Ectonus technique	3	6
E.C.T. unmodified	1	2

In view of the divergence of opinions regarding the best ways of administering electroplexy, it was decided to carry out an empirical investigation into their relative merits.

II METHOD

(i) *Selection and Description of Patients*

The patients were consecutive admissions with schizophrenic and affective disorders to a disturbed male admission ward between August, 1957 and August, 1958. One hundred and twenty-six patients were included in the scheme, and each patient received not less than 5 and rarely more than 20 individual treatments depending upon diagnosis and response to E.C.T. which was given three times per week.

The diagnosis of each patient was based on the clinical impression of the admitting doctor, and an interview by one of us (J.C.B.). Seventy-eight of the patients were diagnosed as suffering from schizophrenia, and 48 were classified as affective conditions (mania, manic-depressive psychosis and depression).

(ii) *Treatment Techniques*

The four most popular techniques given in Table I, together with the technique in current use at this hospital, namely Ectonus E.C.T. with Brevdil "E", were compared. At the outset of the scheme it was not considered justifiable to use "straight" unmodified E.C.T. because of the risk of causing unnecessary fractures. The techniques used were designated A, B, C, D, and E, and were as follows:

"A" *E.C.T. modified with Thiopentone Sodium ("Pentothal") and Succinyl Choline Chloride ("Scoline")*.

The anaesthetic and relaxant were administered intravenously in separate syringes. An hypnotic rather than an anaesthetic dose of Pentothal was used, consisting of 150–300 mg. according to body weight. The dose of Scoline was 20–50 mg. according to weight.

"B" *E.C.T. modified with Thiopentone Sodium and Suxethonium Bromide (Brevdil "E")*.

The relaxant was given in a separate syringe in a dose of 1.0 to 1.25 mg. cation per kg. of body weight, as recommended by the manufacturers (100 mg. of the cation is contained in 150 mg. of the total salt).

"C" *Ectonus E.C.T., without relaxants, using the Ectron apparatus.*

This technique was originally described by R. J. Russell (6).

"D" *E.C.T. modified with Suxethonium Bromide (Brevdil "E") alone.*

The dosage was similar to technique "B".

"E" *Ectonus E.C.T. with Suxethonium Bromide (Brevdil "E")*.

In techniques A, B and D, a single electrical stimulus was applied, which was the current practice at most hospitals (1). In techniques A and B, in order to ensure the maximum modification of the convulsion, the stimulus was not applied until the fasciculation induced by the relaxant had extended throughout the body, and was tending to pass off. In techniques D and E, the shock was given when fasciculation was established in the face and upper limbs, or as soon as there was objective evidence of discomfort, whichever came first. Atropine 1/100 gr. was given subcutaneously thirty minutes before techniques A and B, and with both these techniques oxygen was administered under positive pressure with the Lucas breathing apparatus, immediately prior to the electrical stimulus.

The same routine was adopted for all patients on treatment mornings. They were ushered individually into the treatment room on a stretcher placed upon a trolley, and following E.C.T. were conducted into the recovery room, where the time of regaining consciousness was recorded by a nurse. Efforts were made to reduce changes of nursing staff to a minimum during the period of this investigation.

Patients ineligible for all five techniques were excluded from the scheme. They included those with heart disease and skeletal abnormalities, upon whom the use of E.C.T. without relaxants was considered inadvisable.

The E.C.T. technique used each day was selected on a random basis, so that each patient was unaware of the technique to be used on his next day of treatment. This was done by inscribing the letters A, B, C, D, and E separately on the fronts of five playing cards. The first technique used in the investigation was "A", and that for the next treatment day was decided by shuffling the cards face downwards and removing the top one which indicated the method to be

used. This was continued, using the remainder of the cards, until all the techniques had been given, and constituted a sequence of five treatments. Subsequent sequences commenced with techniques B, C, D, and so on. Altogether there were 24 sequences of five different techniques, covering 120 treatment days.

(iii) *Comparison of Techniques*

(a) *Recovery times.* These were recorded for the different techniques according to the subdivisions enunciated by Little and Reid (5). These are: Phase I, from the stimulus to the cessation of the convulsion. Phase II, from the stimulus to the first breath. Phase III, from the stimulus to the return of consciousness as judged by the patient's ability to respond to simple commands. This last phase was always recorded by the same nurse throughout the entire investigation to minimize error.

(b) *Effects of treatment.* These were registered for the different techniques, and included inadequately relaxed convulsions, difficulty in obtaining a convulsion, excessive restlessness, cyanosis, prolonged apnoea, fractures, headaches, vomiting, the development of confusion, delayed fits, and the loss of front teeth following E.C.T. The necessity for premedication before treatment, and the instances of patients with veins unsuitable for venepuncture were also recorded. All complaints made by patients against the different techniques were carefully noted.

(c) *Patients' preferences.* These were estimated in two ways. (1) By obtaining a global assessment of the preference for different techniques at the completion of the course of treatment, and (2) by calculating the like/dislike ratio between different techniques. With the latter, each patient was asked the morning following each treatment whether he preferred the last technique or the one given previously. No leading questions were posed unless he was undecided, when he would be informed that he had received treatment either without an injection, or with an injection in his arm, or with an injection in his arm which put him to sleep. These suggestions were only necessary in a small minority of patients. Recording was as follows: 2 red marks were given to each technique preferred, and 2 blue marks to each technique disliked by a patient. If he was undecided between techniques, each was given one red and one blue mark. If he remembered one technique only it was given 2 red or 2 blue marks depending upon whether it was pleasant or unpleasant, or 1 red and 1 blue mark if it was indifferent. The results were scored by (a) estimating for each technique the proportion of red to blue marks, and (b) ranking the global preferences for the different techniques at the final interview.

(iv) *Statistical Assessments*

The statistical techniques employed to assess the results varied according to the type of data being evaluated, but were usually either "t" or chi-squared tests. The former were calculated on the assumption of unrelated means and a perusal of the raw data did not indicate that this assumption was incorrect. It should be remembered, however, that, in the event of the means being even slightly correlated, the "t" test for unrelated means would minimize rather than maximize the significance of the difference between them. We can therefore be sure that all significances assessed in this article by the "t" test had at least the statistical significance attached to them in the Tables.

Chi-squared was used whenever possible, in spite of the fact that some of the theoretical frequencies were lower than those usually required for this test. It was not possible, however, to circumvent this problem in an easy manner because of the nature of the raw data. Nor did we see any easy way of satisfactorily manipulating the raw data except by increasing the sample size which was not, in this case, practicable.

Patients' preferences for the treatment technique have been dealt with by the use of the "t" test for the Like/Dislike ratios. The patients' global assessments of techniques have been simply ranked in orthodox fashion and the mean ranks tabulated.

III RESULTS

Phase I recovery times recorded as the time in seconds between the administration of the shock and the end of twitching are set out in Table II together with the critical ratios of differences between the five techniques.

TABLE II

Means and Significance of Differences for Phase I Recovery Times

N=150

		Treatment Technique				
		A	B	C	D	E
Mean time in seconds	..	33.0	33.4	41.3	37.9	39.0
σ		14.2	12.6	17.4	7.7	9.7
Treatment Technique	A	.. ()	NS	**	**	**
	B	..	()	**	**	**
	C	..		()	*	NS
	D	..			()	NS
	E	..				()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

Phase II recovery times are given in Table III. These represent the time in seconds between the shock and the onset of respiration. The statistical significance of the differences between the five techniques are also given.

TABLE III

Means and Significance of Differences for Phase II Recovery Times

N=150

		Treatment Technique				
		A	B	C	D	E
Mean time in seconds	..	86.1	78.1	45.0	69.3	81.6
σ		47.2	21.0	24.5	24.7	25.5
Treatment Technique	A	.. ()	NS	**	**	NS
	B	..	()	**	**	NS
	C	..		()	**	**
	D	..			()	**
	E	..				()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

Phase III recovery times, the time in minutes between shock and recovery of consciousness, together with the statistical significance of the differences between the five techniques are given in Table IV.

TABLE IV

Means and Significance of Differences for Phase III Recovery Times

N=150

					Treatment Technique				
					A	B	C	D	E
Mean time in minutes ..					9.9	9.7	7.0	7.6	7.5
σ					3.3	3.9	3.8	4.0	4.1
Treatment Technique	A	..	()			NS	**	**	**
	B	..				()	**	**	**
	C	..					()	NS	NS
	D	..						()	NS
	E	..							()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

Table V gives the average time in minutes required to give each patient his treatment (including mixing the solutions). It is obtained by dividing the total amount of time spent in administering treatment each day by the number of patients treated. The significances of the differences between the techniques in this respect are also given.

TABLE V

Means and Significance of Differences for Times Required for Treatment Administration

N=20 (days)

					Treatment Technique				
					A	B	C	D	E
Time in minutes per patient					5.6	5.7	3.5	5.3	5.4
σ					1.7	2.2	.82	1.6	1.7
Treatment Technique	A	..	()			NS	**	NS	NS
	B	..				()	*	NS	NS
	C	..					()	**	*
	D	..						()	NS
	E	..							()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

The frequencies of a number of effects of treatment for each treatment technique are given in Table VI together with statistical assessments of the differences.

TABLE VI

Frequencies of Variables Associated with Treatment for Whole Group

N=126

Variable	Treatment Technique					χ^2 All Groups	Significance of Differences									
	A	B	C	D	E		AB	AC	AD	AE	BC	BD	BE	CD	CE	DE
0 No. of treatments ..	257	259	262	243	264											
1 Premedication ..	18	18	25	18	15	NS										
2 Complaints ..	0	0	0	0	0	NS										
3 Not relaxed ..	24	19	omit	36	8	<1%	////	**	////	**	*	////	////	**		
4 Restless ..	21	11	46	38	28	<1%	**	**		**	**	**	*		*	
5 Cyanosis ..	17	10	0	31	50	<1%	**	*	**	**	**	**	**	**	*	*
6 Apnoea ..	3	0	0	0	5	<1%							*		*	*
7 Fractures ..	0	0	4	0	1	5%	*			*				*		
8 Headaches ..	19	12	42	11	19	<1%	**			**				**	**	
9 Vomiting ..	5	1	4	1	3	NS										
10 Vein difficulty ..	10	15	omit	13	8	NS	////				////			////	////	
11 Fit difficulty ..	1	0	2	1	0	NS										
12 Confusion ..	44	40	48	43	42	NS										
13 Delayed fits ..	0	0	3	0	0	NS										
14 Loss of teeth ..	0	0	0	1	1	NS										

//// Not applicable

** Significant at 1 per cent. level or beyond.

* Significant at between 5 per cent. and 1 per cent. levels.

In Tables VII to XI the statistical assessments for the whole group split into diagnostic and age subdivisions are presented.

TABLE VII

Frequencies for Variables in Table VI for All Patients Subdivided by Diagnosis

Schizophrenia (N=78)

Variable	Treatment Technique					χ^2	Significance of Differences									
	A	B	C	D	E		AB	AC	AD	AE	BC	BD	BE	CD	CE	DE
0 ..	185	191	185	181	181											
1 ..	14	14	17	12	11	NS										
2 ..	0	0	0	0	0	NS										
3 ..	17	17	omit	34	7	<1%	////	*	*	////	*	*	////	////	**	
4 ..	19	8	32	28	22	<1%	*	*	**		**	**	**			
5 ..	10	1	0	18	30	<1%	**	**		**		**	**	**	*	*
6 ..	2	0	0	0	3	NS										
7 ..	0	0	3	0	1	NS										
8 ..	8	7	29	6	12	<1%	**			**				**	**	
9 ..	2	0	2	0	1	NS										
10 ..	7	11	omit	11	6	NS	////				////			////	////	
11 ..	0	0	1	0	0	NS										
12 ..	38	33	41	39	38	NS										
13 ..	0	0	1	0	0	NS										
14 ..	0	0	0	1	0	NS										

//// Not applicable

** Significant at 1 per cent. level or beyond.

* Significant at between 5 per cent. and 1 per cent. levels.

TABLE VIII

Frequencies for Variables in Table VI for All Patients Subdivided by Diagnosis

Affective (N=48)

Variable	Treatment Technique					χ^2	Significance of Differences									
	A	B	C	D	E		AB	AC	AD	AE	BC	BD	BE	CD	CE	DE
0	72	68	77	62	83											
1	3	4	8	6	4	NS										
2	0	0	0	0	0	NS										
3	7	2	omit	2	1	NS										
4	2	3	14	10	6	<1%	////	**	**		////			////	////	
5	7	9	0	13	20	<1%		*		*	*	**		**	**	*
6	1	0	0	0	2	NS										
7	0	0	1	0	0	NS										
8	11	5	13	5	7	NS										
9	3	1	2	1	2	NS										
10	3	4	omit	2	2	NS	////				////			////	////	
11	1	0	1	1	0	NS										
12	6	7	7	4	4	NS										
13	0	0	2	0	0	NS										
14	0	0	0	0	1	NS										

//// Not applicable

** Significant at 1 per cent. level or beyond.

* Significant at between 5 per cent. and 1 per cent. levels.

TABLE IX

Frequencies for Variables in Table VI for All Patients Subdivided by Age

<30 Years (N=37)

Variable	Treatment Technique					χ^2	Significance of Differences									
	A	B	C	D	E		AB	AC	AD	AE	BC	BD	BE	CD	CE	DE
0	101	94	92	93	95											
1	10	11	12	14	10	NS										
2	0	0	0	0	0	NS										
3	7	9	omit	17	5	5%	////	*			////			////	////	**
4	9	3	10	12	8	NS										
5	5	1	0	5	13	<1%		*		*			**	*	**	
6	3	0	0	0	1	NS										
7	0	0	0	0	0	NS										
8	9	6	15	4	10	NS										
9	0	0	1	0	0	NS										
10	5	4	omit	7	5	NS	////				////			////	////	
11	0	0	1	0	0	NS										
12	21	16	20	21	17	NS										
13	0	0	0	0	0	NS										
14	0	0	1	0	0	NS										

//// Not applicable

** Significant at 1 per cent. level or beyond.

* Significant at between 5 per cent. and 1 per cent. levels.

TABLE X

Frequencies for Variables in Table VI for All Patients Subdivided by Age

30-50 Years (N=64)

Variable	Treatment Technique					χ^2	Significance of Differences											
	A	B	C	D	E		AB	AC	AD	AE	BC	BD	BE	CD	CE	DE		
0	142	140	146	136	134													
1	13	11	18	7	7	NS												
2	0	0	0	0	0	NS												
3	14	8	omit	21	4	<1%	////				////	*		////	////		*	
4	12	8	33	27	16	<1%	**	**			**	**				*		
5	6	4	0	18	19	<1%	*	**	**	*	**	**	**	**	**			
6	1	0	0	1	1	NS												
7	0	0	2	0	1	NS												
8	10	7	22	8	9	5%	*				**			*	*			
9	5	1	2	1	2	NS												
10	5	6	omit	3	2	NS	////				////			////	////			
11	1	0	1	0	0	NS												
12	22	25	20	20	24	NS												
13	0	0	3	0	0	NS												
14	0	0	1	0	0	NS												

//// Not applicable

** Significant at 1 per cent. level or beyond.

* Significant at between 5 per cent. and 1 per cent. levels.

TABLE XI

Frequencies for Variables in Table VI for All Patients Subdivided by Age

> 50 Years (N=25)

Variable	Treatment Technique					χ^2	Significance of Differences											
	A	B	C	D	E		AB	AC	AD	AE	BC	BD	BE	CD	CE	DE		
0	42	43	49	39	58													
1	2	1	1	2	1	NS												
2	0	0	0	0	0	NS												
3	3	2	omit	1	0	NS	////				////			////	////			
4	0	0	4	0	4	NS												
5	7	5	0	11	21	<1%	*				*		**	**	**			
6	1	0	0	0	3	NS												
7	0	0	2	0	0	NS												
8	4	0	4	2	1	NS												
9	0	0	1	0	0	NS												
10	0	5	omit	3	1	NS	////				////			////	////			
11	1	0	0	1	1	NS												
12	6	6	12	3	6	NS												
13	0	0	0	0	0	NS												
14	0	0	0	0	1	NS												

//// Not applicable

** Significant at 1 per cent. level or beyond.

* Significant at between 5 per cent. and 1 per cent. levels.

Data regarding patients' preferences for treatment are given in Tables XII to XXI. In these Tables the total group of patients has been subdivided again by age and by diagnosis.

TABLE XII

Average Like/Dislike Ratio for Each Technique with Statistical Assessment of the Differences

N=63

				Treatment Technique				
				A	B	C	D	E
Mean ratio	..	..	..	2.41	1.58	1.18	1.16	.83
σ	..	..	..	2.17	1.35	1.46	1.11	.65
Treatment Technique	A	..	()		**	**	**	**
	B	..			()	NS	*	**
	C	..				()	NS	*
	D	..					()	*
	E	..						()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XIII

Average Like/Dislike Ratio for Each Technique for Schizophrenic Patients with Statistical Assessment of the Differences

N=39

				Treatment Technique				
				A	B	C	D	E
Mean ratio	..	..	..	2.12	1.44	1.08	1.07	.85
σ	..	..	..	1.81	1.26	.97	.73	.57
Treatment Technique	A	..	()		*	**	**	**
	B	..			()	NS	NS	**
	C	..				()	NS	NS
	D	..					()	NS
	E	..						()

NS — Not significant.

** — Significant at 1 per cent. or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XIV

Average Like/Dislike Ratio for Each Technique for Affective Patients with Statistical Assessment of the Differences

N=24

				Treatment Technique				
				A	B	C	D	E
Mean ratio	..	..	..	2.86	1.80	1.35	1.29	.78
σ	..	..	..	2.59	1.46	2.01	1.53	.77
Treatment Technique	A	..	()		*	**	**	**
	B	..			()	NS	NS	**
	C	..				()	NS	NS
	D	..					()	NS
	E	..						()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XV

Average Like/Dislike Ratio for Each Technique for Patients Under 40 Years with Statistical Assessment of the Differences

N=42

					Treatment Technique				
					A	B	C	D	E
Mean ratio	..	..	..	..	2.54	1.60	1.20	1.29	.72
σ	..	..	..	..	2.33	1.46	1.63	1.12	.39
Treatment Technique	A	..	()			**	**	**	**
	B	..			()		NS	NS	**
	C	..					()	NS	*
	D	..						()	**
	E	..							()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XVI

Average Like/Dislike Ratio for Each Technique for Patients Over 40 Years with Statistical Assessment of the Differences

N=21

					Treatment Technique				
					A	B	C	D	E
Mean ratio	..	..	..	..	2.13	1.55	1.15	.90	1.03
σ	..	..	..	..	1.79	1.16	1.05	1.05	.97
Treatment Technique	A	..	()			NS	**	**	**
	B	..			()		NS	NS	NS
	C	..					()	NS	NS
	D	..						()	NS
	E	..							()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XVII

Mean Ranks of Patients' Global Preferences for Technique and Significance of Differences

N=63

					Treatment Technique				
					A	B	C	D	E
Mean rank	..	..	..	..	2.5	2.5	3.7	3.1	3.1
σ	..	..	..	..	.78	.57	1.22	.48	.37
Treatment Technique	A	..	()			NS	*	**	**
	B	..			()		*	**	**
	C	..					()	NS	NS
	D	..						()	NS
	E	..							()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XVIII

Mean Ranks for Global Preferences of Patients Over 40 Years of Age and Significance of Differences

N=21

					Treatment Technique				
					A	B	C	D	E
Mean rank	..	..	..	..	2.6	2.6	3.5	3.1	3.1
σ	..	..	..	..	.65	.65	1.37	.45	.45
Treatment Technique	A	..	()		NS	*	**	**	**
	B	..			()	*	**	**	**
	C	..					()	NS	NS
	D	..						()	NS
	E	..							()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XIX

Mean Ranks for Global Preferences of Patients Under 40 Years of Age and Significance of Differences

N=42

					Treatment Technique				
					A	B	C	D	E
Mean rank	..	..	..	..	2.6	2.6	3.7	3.1	3.1
σ	..	..	..	..	.80	.81	1.17	.67	.68
Treatment Technique	A	..	()		NS	*	*	**	**
	B	..			()	*	*	**	**
	C	..					()	**	**
	D	..						()	NS
	E	..							()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XX

Mean Ranks for Global Preferences of Schizophrenic Patients and Significance of Differences

N=39

					Treatment Technique				
					A	B	C	D	E
Mean rank	..	..	..	..	2.6	2.6	3.6	3.1	3.1
σ	..	..	..	..	.60	.61	1.29	.52	.52
Treatment Technique	A	..	()		NS	*	**	**	**
	B	..			()	*	**	**	**
	C	..					()	**	**
	D	..						()	NS
	E	..							()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

TABLE XXI
Mean Ranks for Global Preferences of Affective Patients and Significance of Differences

N=24

				Treatment Technique				
				A	B	C	D	E
Mean rank	..	..	..	2.6	2.6	3.9	3.0	3.0
σ	..	..	..	.58	.57	1.31	.39	.40
Treatment Technique	A	..	()		NS	**	**	**
	B	..			()	**	**	**
	C	..				()	**	**
	D	..					()	NS
	E	..						()

NS — Not significant.

** — Significant at 1 per cent. level or beyond.

* — Significant at between 5 per cent. and 1 per cent. levels.

IV DISCUSSION OF RESULTS

As might have been expected, it is far quicker for the psychiatrist to administer electroplexy when anaesthetics and relaxants are not used. The total times required to complete treatment (Table V) using Pentothal and a relaxant, or a relaxant alone, were both significantly longer than when it was given unmodified. The times taken to give E.C.T. with and without anaesthesia were not significantly different. Although important, time should not be the doctor's primary consideration in the choice of an electroplexy technique, especially when the disadvantages of unmodified treatment may outweigh its other benefits.

(a) *Recovery times.* Phase I was significantly prolonged (Table II) by unmodified E.C.T. compared with all the other techniques, and was significantly shorter in the group receiving anaesthetics than those having relaxants alone. By contrast, Phase II (Table III) was lengthened when anaesthetics and relaxants were used, confirming that these drugs significantly delay the return of respiration. The results shown in Table IV indicate that Phase III was significantly prolonged when Pentothal was given compared to the other techniques. With this phase the differences between the unmodified group and those receiving relaxants alone were not significant.

As far as Phase I is concerned, these findings are opposed to those of Little and Reid (5), who noticed the prolongation of this phase after Scoline. The results, however, accord with those reported by these writers with respect to Phases II and III.

(b) *Effects of treatment.* The patients receiving the Ectonus technique with Brevidil "E" had significantly more well relaxed fits than those given all other modified techniques, confirming the advantages of Ectonus over the instantaneous stimulus in smoothing out the convulsion. The results of this study supported the observations of Havens (4), that restlessness occurred significantly more frequently after the unmodified technique, and also indicated that when anaesthetics and relaxants were combined there was significantly less post-E.C.T. restlessness than when relaxants were given by themselves.

By contrast, cyanosis requiring oxygen administration occurred signifi-

cantly less frequently after unmodified E.C.T. compared with the other techniques, but headaches were significantly more frequent after unmodified treatment.

Fractures, as might have been expected, were more numerous after unmodified treatment, although the difference between unmodified E.C.T. and Ectonus with Brevdil "E" in this respect just failed to reach statistical significance. Five mid-dorsal fractures, confirmed by X-ray, occurred during the investigation. Four followed the unmodified technique, and one followed Ectonus E.C.T. with Brevdil "E", in a patient who appeared to have a well-relaxed fit. There was no evidence of any residual disability. A few patients complained of temporary back pain following unmodified treatment, but this was not sufficiently severe to warrant radiological examination.

There were eight instances of prolonged apnoea following relaxants during the investigation. Apnoea following Ectonus E.C.T. with Brevdil "E" occurred significantly more frequently than with the other techniques. The majority were fortunately of only a few minutes duration with normal recovery, but one patient did not breathe spontaneously for one hour following Ectonus E.C.T. with Brevdil "E", and showed severe depression of the serum pseudocholinesterase level. His case has previously been reported (2). The remainder showed only slightly depressed or normal serum pseudocholinesterase levels, implying that the apnoea was induced by other mechanisms (2). It was also observed that apnoea was frequently repeated in the same patient undergoing successive treatments, and in this series appeared to be unrelated to age.

None of the other recorded effects of treatment proved to be statistically significant.

When the whole group of patients were subdivided into smaller groups according to diagnosis (Tables VII and VIII) or to age (Tables IX, X, and XI) the incidence of treatment effects did not prove to be essentially different.

(c) *Patients' preferences.* In contrast to the findings of Havens (4), the results from both the global interview (Table XVII) and the like/dislike ratios (Table XII) indicated that a significantly larger proportion of our patients favoured E.C.T. given with an anaesthetic. Interesting differences were noticed using the different methods of obtaining preference with regard to unmodified techniques and those in which relaxants were administered alone. The global preference indicated that unmodified E.C.T. was the most unpopular technique, whereas the results of the like/dislike ratios implied that significantly more patients preferred this method to E.C.T. modified with Brevdil "E" without anaesthesia. This may well be associated with unpleasant suffocating sensations with the latter technique, vividly impressed upon the patient's memory, which have been forgotten at the time of the final interview because of E.C.T. confusion.

The possibility of obtaining a discrepancy in the results of patients' preferences for techniques, which is clearly dependent upon the method of obtaining the patients' preferences, should always be borne in mind in this type of investigation. Because of the confusion following a course of E.C.T. we would suggest that the paired preference technique has more value than the patient's global assessment on completion of his E.C.T. course, and therefore that the patient's preference for unmodified E.C.T. is greater than his preference for E.C.T. with relaxants alone.

Subdivisions of the total group by age and by diagnosis (Tables XIII, XIV, XV, XVI, and XVIII, XIX, XX, and XXI) give results which are not essentially different from the whole group.

V CONCLUSIONS

Whilst other studies (4, 7) have shown no significant differences in the long-term therapeutic effectiveness of modified versus unmodified E.C.T., this investigation was constructed to examine the immediate merits and demerits of different electroplexy techniques. A comparison of these techniques shows that all have advantages and disadvantages with which the psychiatrist must be familiar. The risk of fractures following the unmodified technique is perhaps the most serious disadvantage of all.

In the absence of differential long-term therapeutic effects of modified and unmodified treatment, and in view of the present data which are conflicting for the criteria tested, it would appear that the patient's own preference should be given careful consideration. This, according to our data, is for electroplexy administered under anaesthesia, whilst the addition of a relaxant will reduce the possibility of the occurrence of fractures. These results imply that an anaesthetist should *always* be available during treatment sessions, which is not at present the case (1).

For the patient requiring E.C.T. at out-patient clinics it may be considered advisable to administer electroplexy without anaesthetics which significantly delay the return of consciousness, so as to enable patients to return home or to work in the shortest possible time. It should be remembered, however, that the duration of unconsciousness, although longer for electroplexy given under anaesthesia is longer by only three minutes—a difference which might be considered negligible.

VI SUMMARY

Five different electroplexy techniques have been compared, using 126 male patients with diagnoses of schizophrenia or affective psychosis.

The results suggest that patients' preferences ought to be given consideration in deciding the choice of treatment technique.

The patients in this study consistently chose to have their electroplexy under anaesthesia, while the administration of a relaxant in addition will reduce the possibility of fracture.

VII ACKNOWLEDGMENTS

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THE CONCEPT OF "DYNAMIC" CONSCIOUSNESS

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INTRODUCTION

THE nature of consciousness is a central theoretical problem for psychology, psychiatry and psychosomatic medicine. Attempts to deal with this problem in these fields have led to precarious relationships with philosophy on the one hand and with neurophysiology on the other. The result is both conceptually and semantically unsatisfactory. For example, is "consciousness" to be taken to mean some general state or level of awareness which is capable of being altered or reduced? Or is there no general consciousness but only states of being conscious of specific things? This paper discusses some of the philosophical problems involved in the term "consciousness" and outlines ways in which recent neurophysiological advances have contributed to clinical knowledge about the general or specific nature of consciousness.

PHILOSOPHICAL ASPECTS

Most of the difficulties concerning the term "consciousness" have arisen from its introspectionist origins. William James, for example, in the introduction to his *Principles* (1890) makes the introspectionist approach a dogma when he states:

"Introspective observation is what we have to rely on first and foremost and always. The word 'introspection' needs hardly to be defined—it means of course looking into our own minds and reporting what we there discover. Everyone agrees that we there discover states of consciousness. So far as I know the existence of such states has never been doubted by any critic, however sceptical in other respects he may have been. That we have cogitations of some sort is the *inconcussum* in a world most of whose other facts have at some time tottered in the breath of philosophical doubt. All people unhesitatingly believe that they feel themselves thinking and that they distinguish the mental state as inward activity or passion from all the objects with which it may cognitively deal. I regard this belief as the most fundamental of all the postulates of Psychology and shall discard all curious enquiries about its certainty as too metaphysical for the scope of this book."

In spite of James's enviable certainty, developments in psychology since his day seem to have stemmed from various forms of doubt about this very *inconcussum*.

There are two kinds of objection to this introspectionist formulation. These can be referred to as the subjectivist fallacy and the fallacy of misplaced concreteness. The former is the metaphysician's objection to the idea of self-consciousness as a cognitive state which has itself as its own object. This is

held to be a psychological impossibility as every cognitive state must have for its object something other than itself (Baldwin, 1925).

The fallacy of misplaced concreteness appears to be more fundamental. It denotes the objection to ascribing concrete characteristics to an abstraction. Introspection leads us into this error because it makes available to us certain processes or experiences which have characteristics in common. We abstract this common character and call it "consciousness" and subsequently take the original experiences to be "states" or "modifications" of consciousness. This objection is more likely to worry the philosopher than the psychologist or clinician who, in trying to be scientific about consciousness, are dealing with conventions similar to those in the physical sciences. In dealing with things we start from an abstraction of their common property which we term "matter" and then talk as if the things themselves were forms of matter.

The development of the associationist school of philosophy tended to widen the original introspectionist use of "consciousness". For example, Bertrand Russell in his *Outline of Philosophy* (1927) describes consciousness and its operation in the processes of perceiving, involving physical processes external to the body, then processes in the eye, nerves and brain, producing finally a pattern which by the law of association gives rise to tactual and other expectations and images as well as memories and other habits.

"But everything in this whole series consists of causally continuous change of events in space-time, and we have no reason to assert that the events in us are so very different from the events outside us—as to this, we must remain ignorant since the outside events are only known as to their abstract mathematical characteristics, which do not show whether these events are like thoughts or unlike them."

This point of view allows Russell to state the practical functions of consciousness and thought to be "that they enable us to act with reference to what is distant in time or space, even though it is not at present stimulating our senses" (*Analysis of Mind*, 1921).

The philosophers' process of hardening themselves against the ghostly notion of mind has been carried furthest by Ryle (1949) who rejects the notion of consciousness or of a mind as an entity of some sort, just as brain, a hand or a nose is an entity. Originally mind was thought of as a queer mysterious entity as indicated by the terms which have been used as synonyms, such as soul, ego and psyche. Ryle argues that mind is neither mysterious nor an entity and that, as before, its mystery arises from our tendency to treat an abstraction as though it were concrete. Ryle's treatment of the problem can be summarized in the following simple example.* We know that if we bend a piece of wood sufficiently hard it will break. We can therefore say of this piece of wood that it has a tendency to break. Saying that the wood has a tendency to break is not like saying that a man has a brain, a hand or a nose, for there is no such entity as a "tendency to break". To say that the piece of wood has a tendency to break is merely to state that if certain conditions are fulfilled then it is likely that the wood will break. Ryle suggests that to say that a person has a mind is similar to saying that the wood has a tendency to break. Thus the mind or consciousness is not to be thought of as an entity but as a complex of dispositions. To say that a person has a mind therefore does not mean that in addition to his body there is a ghostly something, i.e. his mind, known only to himself and to

* I am indebted for this example to Professor Smart of the University of Sydney.

others by hearsay only. It means that his body has a complex set of dispositions to behave in various ways. Thus Ryle can conclude that "mind is not the topic of sets of untestable, categorical propositions but the topic of sets of testable, hypothetical and semi-hypothetical propositions".

This kind of argument is psychologically acceptable and can take us out of philosophy. The psychological version is that we know about the mental capacities of an organism by knowing about the properties of the organism. This however, raises the question of what properties an organism must have to make it appear with any reasonable degree of certainty to be a conscious human being. It is possible to tackle this question without paying attention to the basic mechanisms of the bodily dispositions. For example, Skinner (1938) in his operationist approach deals with the properties of the empty organism and intentionally ignores the nervous system. To Skinner the properties of the organism are simply the ways in which stimulation and response are connected, just as the properties of any electronic instrument are the ways in which the electric output is related to the electric input. However attractive this simple solution may be, Skinner still uses the process of introspection as a psychological property of living human organisms and we are thus brought back to the previously mentioned difficulties of the confusion of consciousness meaning awareness of environment and consciousness meaning awareness of mental processes themselves.

CLINICAL ASPECTS

Cobb (1952) on the other hand, ignoring these difficulties and using the term to mean both awareness of environment and of self, holds that consciousness must be something more than response to stimulation because a response can occur at spinal levels at which no awareness is involved. Cobb's argument introduces the neural implications of the bodily dispositions which Ryle attaches to "mind", for he asserts right away that consciousness is a property of the organism in action just as much as contraction is a property of muscle. It is a physiological function and as such is associated with a system of organs—specifically the central nervous system. The central nervous system represents a hierarchy of more and more complex neural mechanisms and consciousness is integrated at many levels, dependent upon the existence of reverberating circuits between cortex and thalamus and relationships between cord, brain stem, hypothalamus, thalamus and cortex. The core of Cobb's argument can be stated in three propositions which he holds to be valid for the contemporary state of knowledge:

- (a) No biological process occurs without involving a change in structure.
- (b) Whenever the brain functions there is organic change.
- (c) The brain is the organ of mind.

We have reached a point at which we have apparently resolved many of the philosopher's problems by an assertion that psychological phenomena such as thinking, knowing, willing are just as much functions of the organism as are walking, excreting, digesting, for there are no other kinds of function—unless supernatural. This may not be an entirely satisfactory position to maintain but it serves to translate the problem into the clinician's field which deals with phenomena related to illness and disease processes.

It might be expected that the neurologist's views on consciousness would arise from an entirely different set of determinants from those of the philosopher. This may not be entirely so, for Riese (1954) claims that Cartesian

dualism and Evolutionism were the two greatest influences in the development of Hughlings Jackson's and consequently of contemporary neurology. The significance of evolutionary thought seems obvious enough in Jackson's concept of hierarchy and the Cartesian philosophy may have determined his acceptance of a mind-body dichotomy as exemplified in his often quoted assertion that "there is no physiology of the mind any more than there is psychology of the nervous system". Certainly, although from different premises, he arrives at statements which have the characteristic Cartesian stamp of separating subject and object. For example, although the highest cerebral centres were to Jackson the physical basis of consciousness, he postulated that the substrata of consciousness were double. By the nervous arrangements of the right posterior and left anterior lobes he maintained that we learn the nature and position of the object which affects us. The nervous arrangements of the right anterior and left posterior lobes allowed us to learn the manner in which our organism is affected. He further elaborated the distinction between subject and object consciousness by claiming that the activity of the substrata of subject consciousness always preceded that of the substrata of object consciousness which were thus higher in his hierarchy than those of subject consciousness.

From Jackson's work we derive the concept of functional levels in the central nervous system on which we base our ideas of the supremacy of cerebral cortex, equating higher mental processes with higher levels of brain function. In the search for a "location" for consciousness there was a tendency to ignore lower or brain-stem centres as being of subsidiary importance and under the control of the more recently developed cortex.

Head (1926) however did not concentrate only upon higher centres. He held that consideration of lower functional levels of nervous system could throw a light on the nature and significance of consciousness for even in decerebrate preparations such as a spinal cat, for example, a great degree of adaptative behaviour can occur. Head originally developed a concept of vigilance to apply mainly to spinal and mid-brain levels but by analogy it came to refer to the operation of cerebral cortex on the basis that consciousness has the same relationship to the higher nervous centres as purposive reflexes have to lower nervous centres. Vigilance referred to the high-grade state of physiological efficiency of any level of nervous system and "when vigilance is high mind and body are poised in readiness to respond to any event, external or internal, but if it is lowered by injury, want of nutrition, chloroform or any other toxic influence, those high-grade functions may suffer in general or in part whether they are associated with consciousness or not". The last part of this quotation should be stressed to disaffirm that Head equated consciousness with vigilance.

The clinically based approach to consciousness starts from considerations of unconsciousness as a symptom. This negative term presents as many difficulties as the positive term and Jefferson (1944) feels that a new term is needed to define unconsciousness—traumatic or otherwise—which would designate more pointedly its nature and its pathological status in terms of neurophysiology. However, to do this a large number of terms would be required as unconscious patients differ profoundly in respect of such factors as the degree of unconsciousness, whether consciousness is lost fully or only in part, whether it is transient and fleeting or prolonged and involves coma.

Martin (1949) distinguishes two varieties of unconsciousness and disturbed consciousness: (a) coma—related to sleep and to depressed cortical activity and (b) convulsive—related to irregular cortical discharges. He states that there

appears to be no evidence of consciousness in man from the activity of other structures in the absence of cortical activity and that an impairment of activity of cortex over a wide area leads to unconsciousness. However, this activity of cortex is maintained in some vegetative fashion by the activity of the hypothalamus and unconsciousness may be caused by lesions of the hypothalamus.

In this Martin seems to be merely restating the view that the activity of the cortex with which consciousness is associated is maintained by afferent impulses in sensory systems. However, he goes on to suggest that consciousness depends not only upon a process in which the cortex is kept in a state of activity by sensory impulses but also by an endogenous activation dependent upon the hypothalamus. The hypothalamus appears to be the driving influence of the cortex and is likened to the electric current which makes the wireless set live. Once the cortex is live it is capable of receiving and of interpreting sensory excitations without which the cortex is silent and consciousness cannot be demonstrated. This means that, although in theory consciousness might be maintained by tactile, olfactory, gustatory, auditory and visual impulses arising from the environment, some excitation from the body itself is essential for the maintenance of consciousness. This modifies the assumption of a direct correspondence between "higher mental processes" and "higher nervous levels". The statement can still be made that consciousness is associated with the activity of the cortex which is of course different from saying that consciousness is an activity of the cortex.

Brain (1950) also suggests that subcortical structures have an important role to play in the maintenance of consciousness:

"Consciousness is linked with basal nuclei which made their appearance in the course of evolution millions of years before thought became possible, and since the days of our earliest vertebrate ancestors have sustained the life of the feelings."

Statements of this kind which direct attention to the importance of non-cortical structures for consciousness are precursors of the work on the ascending reticular system which originated "with the chance observation that direct electrical excitation of the reticular formation of the brain stem induced changes in the EEG seemingly identical with those observed in awakening from sleep or alerting to attention" (Magoun, 1954). From this chance observation a great deal of work has developed with interdisciplinary significance. Such work is reported currently in an International Symposium of the Henry Ford Hospital (Jasper, 1958) and previously in a symposium sponsored by the Council of the International Organization of Medical Sciences (Delafresnaye, 1954).

THE SIGNIFICANCE OF THE BRAIN-STEM RETICULAR FORMATION

The reticular system of the brain stem is an ill-defined anatomical entity, histologically primitive and undifferentiated and well-developed in amphibious animals (Nauta and Whitlock, 1954). In the primates the system acts in conjunction with the diffuse thalamic projections to the cortex (Moruzzi and Magoun, 1949).

Cajal at the beginning of this century had observed significant differences in the reticular cells of the brain stem involving both sensory and motor collaterals and had concluded that not only do such cells have multiple influences operating upon them but even adjacent cells may have entirely different connections (Livingston, 1957). However, by the methods of study then

available the brain-stem reticular system was generally found to be either unresponsive to stimulation or to yield apparently non-specific patterns of response.

This finding was of course not in keeping with the spirit of neurophysiological research which was until recent times dominated by localization hypotheses and sought more refined knowledge of point-to-point relationships within the nervous system. Magoun (1944) and others working on animals without central anaesthesia began to interest themselves in the functions of the reticular formation which seemed to be widespread in their effects. This led to a distinction within the nervous system between two general divisions—one comprising the "classical" sensory and motor pathways with relatively discrete functions and the other including the brain-stem reticular formation which appeared to have more generalized functions.

Moruzzi (1949), Jasper (1949) and Lindsley (1949) reported electrophysiological, neurophysiological and psychophysiological studies which showed that this brain-stem reticular formation had both a widespread inhibitory effect on spinal motor mechanisms and a generalized facilitatory influence. This latter facilitatory function of the reticular formation was referred to an ascending system of projections which tend to activate the cortex in a generalized fashion.

Further, the reticular formation is capable of modifying central excitatory states in a downwards direction. Livingston (1957) has shown that the cortex projects from certain discrete areas down into the reticular formation producing not only an interaction between descending impulses from the cortex and the sensory input but also an interaction of certain cortical fields with each other. He uses the term "a kind of Grand Central Station for the interaction of impulses generated in remote parts of the nervous system" to describe the complex activity of the reticular formation.

Thus it seems that certain cortical fields can be influenced in their activity by the intrinsic activity of the brain stem and in their turn these individual cortical fields can exert patterns of influence upon this intrinsic activity either by diminishing or augmenting it. The picture is even more complex when the sequence is shown to produce alternations of excitement and depression of such intrinsic activities. As Livingston (1957) puts it:

"... the cortex is not simply the victim of whatever the reticular activating system might demand of it but the cortex itself possesses corticofugal regulating mechanisms which in turn influence the level of activity within the reticular formation."

Evidence for this is supplied from the experiments of Segundo, Arana and French (1955) working in Magoun's laboratories. They have shown that electrical activation of certain cortical fields in monkeys immobilized by curare but free from the influence of central anaesthetic induces the EEG response characteristic of arousal. Also, naturally sleeping monkeys with implanted electrodes in such cortical fields are awakened and aroused behaviourally when stimulation is applied. However, electrical stimulation of cortical sites which do not project to the reticular formation fails to elicit such EEG arousal or behavioural changes even though high intensities of current are applied. It seems therefore that corticofugal projections play a part in activating the rest of the brain via the reticular activating system. This is held to be so, not only in relation to arousal in response to specific stimuli but also for the maintenance of a centrally "aroused" state.

Investigations of sensory components suggested that the brain-stem reticular formation is also able to influence conduction along sensory paths (Moruzzi, 1956). For some time it has been recognized that recording of EEG changes in response to sensory stimulation was easier from anaesthetized than from unanaesthetized animals. This is attributed to the fact that during anaesthesia the inhibiting action of the reticular formation upon afferent impulses along classical sensory pathways is interrupted. The sensory implications are specifically illustrated in the work of Hernandez-Peon, Scherrer and Jouvett (1956) on unanaesthetized cats with electrodes implanted in the dorsal cochlear nucleus to allow recording of auditory impulses. In the relaxed cat responses to a click could be recorded as a high-amplitude localized electrical discharge. When however some mice in a jar were placed near the cat the amplitude of the discharges in response to the click-stimuli was markedly reduced while the animal's attention was directed to the mice. When the mice were removed and the cat was once more relaxed and inattentive responses to the clicks returned to their previous level.

They also found that if the click-stimulus was repeated and prolonged in the absence of reward or punishment cues the recorded potential was reduced in accordance with the expected sensory adaptation or habituation effect. The interesting theoretical point here is that the psychological assumption that this habituation is perceptually determined is not confirmed as it appears that the sensory pathways, conventionally held to be discrete up to the level of cortex, can in fact be influenced significantly at a level well below cortex by events occurring in the brain stem.

Jung and his colleagues (1958) in Freiburg have used a technique of micro-electrode recordings from single neurones to demonstrate that the subcortical non-specific system can exert its effects on single neurones. Their experiments on light vision show that a general state of alertness or arousal can influence the subjective point of flicker fusion. This has significance for an understanding of perception and how excitation is paralleled in subjective experience.

Such a formulation allows the beginning of an appreciation of how the central nervous system can provide some of the neural mechanisms underlying arousal and consciousness. The activity of the reticular activating system seems to be implicated both in the maintenance of "levels" of consciousness and also, because of its capacity for sensory control, in determining the "content" of consciousness.

DISCUSSION

This does not mean that a locus or "seat" of consciousness has been found. This is philosophically unsatisfactory and is no more meaningful than attempting to ascribe the sound from a wireless set to a switch, a valve or a circuit rather than to operations which can be abstracted from all the components of the set. The neurophysiological work on the reticular activating system extends our psychophysiological concepts so that they become more consistent with the complexity we have come to expect from the neural mechanisms underlying our capacity to adapt or our ability in Russell's words "to act with reference to what is distant in time or space even though it is not at present stimulating our senses". This work also suggests that consciousness should be viewed in a scalar or quantitative fashion along a continuum between coma and "clear" consciousness such as is suggested by Delay (1946) in his assertion that what we know as consciousness in man is an extrapolation of the primitive vigilance shared by a large part of the animal kingdom.

Previous attempts in psychology to formulate a rational basis for the neural mechanism underlying conscious processes have been unsatisfactory in that they have either led to a complete rejection of neurophysiological variables as with Skinner, or of consciousness itself as with the Behaviourists, or to an acceptance of an implicit congruity between psychological and physiological processes as with the Pavlovians. While it may not solve the problem of the "seat" of consciousness, this new neurophysiological approach is a fruitful source of hypotheses and can provide a model of consciousness appropriate to psychology.

A Model of Consciousness

The model of consciousness which can be derived from this work is a system in which complex patterns initiated by an input are controlled by central dominance and in which the direction of this central dominance is determined by some part of the input to the system. Its function in a biological sense is therefore regulatory. In electrical or mechanical terms the system would be a circuit or device whose operation provided a continuous series of equilibria. If we now transfer the regulatory nature of this system to the concept of consciousness itself we can arrive at the notion of "dynamic" consciousness. This term implies that it is no longer appropriate to regard consciousness as passive or epiphenomenal as the conventional stimulus-response approach might suggest.

Although it may be no more than sophistry it is worth while pointing out the paradox that, while we have a concept of dynamic unconscious processes in psychology, we still tend to regard consciousness as a static and intangible quality. The new concepts in neurophysiology can allow us to think of consciousness in more dynamic terms and to say that it is the characteristic whereby an individual's capacity to react adaptively can be maximized. It is akin to such concepts as vigilance, alerting or arousal, although the technical use of these terms does not permit them to be synonyms for consciousness.

The significance of processes of attending in perception parallels the significance of dynamic consciousness for general behaviour in which an adjustment is maintained between the inner processes and environmental change. Hebb (1949, p. 146) makes the point that:

"The most important mark of consciousness is the continual changing selective responsiveness to different aspects of a familiar environment, the unchanging responsiveness to unusual or unexpected events together with the continual presence of purpose . . . or motor equivalence."

However, the concept which is offered here of dynamic consciousness would stress that it is consciousness itself which provides the essential conditions for varying behaviour in an adaptive fashion.

Starting from the simple statement that the more information available to an individual the more likely is his subsequent behaviour to be adaptive, we can use an analogy between perceiving and statistical methods. The more adequate the information sampled the more likely is the resultant action to be appropriate (Collier, 1955). Consciousness, by this analogy, provides the best possible sampling conditions for any required action. This permits the convention of consciousness as a continuum for it is not always appropriate to take the largest possible sampling which is called for under conditions of extreme novelty or threat. An ordinary everyday level of consciousness can be maintained on perceptual sampling well below the maximum possible sampling

capacity. Similarly, disorders of consciousness can be viewed as situations in which the appropriate sample cannot be achieved and the consequent failure to adapt results from behaviour determined by this inadequate sampling. Many psychological symptoms of "organic deficit" can be viewed in this way. However, the danger in such an analogy is that one may think of the operation of dynamic consciousness purely in conventional perceptual terms, i.e. as being solely determined by the environmental cues.

The model of consciousness would of course involve the conventional afferent-efferent dimension, but would add the significant central regulatory mechanism which can produce activation in the absence of an input (i.e. other than interoceptive). As with all biological regulating systems equilibrium is achieved by balancing counter-forces—in this case the activation from perceptual input and the inherent activation of the brain-stem reticular apparatus. This apparatus is capable at one and the same time of alerting the system appropriately in response to stimulation and of balancing the input to the state of alerting achieved. This is consistent with the philosophical interpretation that consciousness represents what we are aware of and also the conditions for our awareness.

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IODINE-132 UPTAKES BY THE THYROID IN PSYCHOTICS

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THE study of thyroid function as the uptake of radioiodine (I^{131}) is a well-established test. Since the half-life of the isotope is long (8 days) it is unreasonable to make frequent repeated tests in the same person because of the cumulative radiation risk and the complexity of interpretation when residual radioactive iodine is still present in the body. However, in psychiatry daily or twice daily measurements of thyroid function might be very useful in studying patients who show sudden or rapid mental changes (Sands, 1958), and a radioiodine isotope with a half-life of only 2.26 hours which has become more readily available (I^{132}), deserves trial. The primary aim of the present work was to make daily measurements on one man through several short (6-day) cycles of behavioural change. He was predominantly manic-depressive in type and has already been described in detail (Crammer, 1959). To discover how variable the measurement could be, repeated observations were also made on a group of 20 chronic male patients living together and showing an unchanging clinical picture. Observations were repeated on them after three months of chlorpromazine treatment to see whether this would have altered the values obtained for thyroid uptake.

METHODS

Preparation of Radioactive Iodine Solution. Alkaline tellurium¹³² sulphate solution obtained from Harwell was treated with acid hydroxylamine and hydrogen peroxide solution. This mixture was distilled in an all-glass micro-distillation apparatus and condensed into alkaline 0.02 normal thio-sulphate solution. About 10 ml. of distillate was used each time and the resultant solution was made isotonic by the addition of a calculated quantity of strong saline solution. Additional physiological saline was added to give the correct activity for the required dose in 1 ml. of saline. The bulk material was distributed in 1 ml. sealed ampoules. These were sterilized for 30 minutes in a boiling water-bath and were used within 1-2 hours of preparation. The dose was drawn from the ampoule into a tuberculin syringe and given into an arm vein.

Counting Techniques. The dose delivered to the patient was taken as the difference between counting rates obtained from the full syringe and from the same syringe after injection. All the counting in these determinations was carried out by means of a ratemeter working from four G 10 Pb Geiger Counters (20th Century) arranged in a square pattern. This arrangement of counters gave a large area in the centre of the square in which the counting rate of the

sample was almost independent of its position. The counters were held in a frame which could be opened and fitted quickly round the patient's neck, at the level of the thyroid, the gland being positioned in the area of uniform sensitivity by bringing the neck forward against a simple cuff fixed to the frame. As a routine it was found convenient to measure the activity in the thyroid (neck) 90 minutes after injection. The count so obtained was corrected for background count and the decay of the radioisotope.

In all cases a standard ampoule was set up at the beginning of the experiment and the decay rate followed throughout the period of the experiment using the counter assembly.

Significance of Results. It was found that the uptake figures obtained in this fashion followed the same pattern as those obtained with Iodine¹³¹, e.g. 20–50 per cent. uptake normal, 60 per cent. and over hyperthyroidism, below 15 per cent. hypothyroidism. The estimated error in the determination is of the order of 3 per cent.

Cases Studied. The 20 men, all between the ages of 30 and 60 and all having been at least 10 years in hospital, were mostly chronic schizophrenics living together in the same open ward. For at least a fortnight before each test all cooking and table salt was "analar" sodium chloride, but no other dietary restriction was enforced. Apart from the period of drug trial, when half of them received chlorpromazine capsules, 300 mg. daily, and the other half identical capsules containing lactose, they received no drugs of any kind, not even the laxatives or cough cures usually provided by the nurses. The intention was to maintain a constant low iodine intake. The cyclical patient was not on any drugs, was in a different ward, and his intake was uncontrolled. All patients were familiarized with the procedure by rehearsals before the actual tests were begun. All tests were carried out between 2 p.m. and 5 p.m. on each test day.

RESULTS

(a) *The Group*

Table I shows the measurements of thyroid activity on four days before the drug trial, and on three days after chlorpromazine treatment had been continued for at least three months. Agreement between the values for 25 and 26 July is in general quite good, except for 7, 9, and 16, 17, 18, who show differences of at least 20 per cent. between the two days. When 29 July is also considered, 6 shows an aberrant value, while 24 October yields at least 8, 10, 14, 16 with values differing from their previous three. These individual variations are unlikely to be due to diet since food was nominally the same for all, while the variation on the same day is an increase for some, a decrease for others (the uniform depression of all values on 21 March is likely to be a dietary effect). Individual variations of this sort have been noted by other workers (Fellinger, Höfer, and Vetter, 1955; Hanbury *et al.*, 1954; Hare and Haigh, 1955; Francois *et al.*, 1958), and require further exploration since their cause is undetermined. For our present purpose, therefore, a finding of no change in iodine uptake during a mental change or chemotherapy would be much more significant than the reverse, which might merely be "spontaneous" variation.

(b) *Effect of Chlorpromazine*

The clinical therapeutic effects will be reported elsewhere (Letemendia and Harris).

TABLE I
Percentage I^{132} Uptakes on Different Days

Patient	25 July	26 July	29 July	24 Oct.	17 Jan.	23 Jan.	21 Mar.
1	29	30	(32)	30	35	41	26
2	33	32	33	33	32	32	23
3	27	28	30	(27)	26	28	24
4	30	32	34	32	30	35	26
5	23	26	25	21	(29)	27	(23)
6	33	33	39	30	33	33	27
7	43	33	43	40	26	32	27
8	27	25	28	34	34	28	25
9	35	28	35	32	35	32	23
10	29	30	34	42	33	25	23
11	31	32	31	24	30	39	23
12	26	26	30	(26)	29	30	23
13	31	28	33	(29)	32	32	23
14	32	27	30	19	30	30	28
15	34	30	35	21	34	27	23
16	32	25	30	16	26	32	23
17	38	29	35	38	44	47	33
18	29	36	35	29	43	38	27
19	23	29	34	31	41	48	31
20	37	34	30	27	40	52	26

Treatment began after 24 October, the first ten receiving placebo, the second ten (below double line) chlorpromazine 300 mg. daily. Figures in brackets are values calculated as described in the text.

TABLE II
Comparison of Average Percentage Uptakes

Date	First Ten	Second Ten	Difference	Standard Error of Difference
25 July	30.8	31.1	+ 0.3	2.27
26 July	29.6	29.4	- 0.2	
29 July	33.4	32.3	- 1.1	
24 October	32.6	25.6	- 7.0	3.26
17 January	31.6	34.7	+ 3.1	
23 January	31.3	37.2	+ 5.9	3.24
21 March	24.7	26.0	+ 1.3	1.25

The second ten received chlorpromazine after 24 October.

Table II compares the observed uptakes of control and treated groups both before and after treatment. The difference between the averages of the two groups must be more than twice the standard error of their difference for the result to be statistically significant. Before treatment the groups compare well, except on 24 October, when, however, the "first ten" comprise nine and the "second ten" only eight observations. After treatment the chlorpromazine group tends to give a slightly greater thyroid activity reading than the controls, but the difference fails to reach significance. However, statistical analysis is handicapped by the unavoidable absence of a few observations. These can be estimated (values in brackets, Table I), by calculating the mean daily percentage uptake for a patient from the available readings and weighting this by a factor derived from the variation between days. Thus the missing observation on 29 July (patient 1) is estimated as:

mean of observation on 25, 26 July and 24 October, for the Patient

Overall mean for first 10 patients on 29 July

$\times \frac{\text{Overall mean for first 10 patients on 25, 26, 29 July, and 24 October}}{\text{Overall mean for first 10 patients on 29 July}}$

Table III shows a comparison of mean differences between the experimental and control groups. In the pre-treatment period the readings are reasonably homogeneous, the control group having a mean daily uptake of 31.5 per cent., compared with the experimental group's 29.9 per cent. (see A). This difference is still well below a reasonable level of significance ($t = .91$, $p = .35$).

TABLE III
Comparisons of the Two Groups

Comparison	n	Mean	D.	t.	P.
A. Control Group (Pre-treatment) ..	10	31.5			
v. Experimental Group (Pre-treatment)	10	29.9	1.6	0.91	<0.4 >0.3
B. Control Group (Post-treatment) ..	10	29.1			
v. Experimental Group (Post-treatment)	10	32.8	3.7	1.89	<0.1 >0.05
C. Control Group (Mean differences between pre-treatment and post- treatment values)	10	2.4			
v. Experimental Group (ditto)	10	- 2.9	5.3	2.77	Significant at <0.02 >0.01
D. Control Group (Pre-treatment) ..	10	31.5			
v. Control Group (Post-treatment) ..	10	29.1	2.4	1.87	<0.1 >0.05
E. Experimental Group (Pre-treatment)	10	29.9			
v. Experimental Group (post-treatment)	10	32.8	2.9	2.17	Significant at <0.05 >0.02

After treatment a straight comparison (B) of the two groups also shows a non-significant difference between means ($t = 1.89$) which suggests that the chlorpromazine treatment has had no effect on iodine uptake. This may be misleading, however, as the trend of the changes in each group has been in opposite directions. The mean uptake for the controls has fallen from 31.5 to 29.1 per cent. (possibly a seasonal change?), whereas for the chlorpromazine-treated it has increased from 29.9 to 32.8 per cent. On the assumption that the two groups would have behaved similarly in the absence of chlorpromazine the difference might be due to treatment. The mean change for the control group (D) is a loss of 2.4 ($t = 1.87$, $p < .1$). The mean change for the chlorpromazine group (E) is a gain of 2.9 ($t = 2.17$, $p < .05$). If a direct comparison of the behaviour of the two groups is made (C), then the difference of the means of the individual changes is 5.3 ($t = 2.77$, $p < .02$), which is quite highly significant.

Thus the effect of chlorpromazine may have been to increase the percentage uptake of I^{132} by a small amount, but if so, the change was of an altogether smaller order than that observed in thyroid disease.

(c) Cyclical Patient

Table IV shows the values obtained through two consecutive and one further cycles. The uptake on 24 October was measured thirty minutes late because on this one occasion the patient was in strange surroundings, became very

TABLE IV
Percentage I^{132} Uptakes in a Cyclical Patient

Mental State	Date	Uptake %	Date	Uptake %	Date	Uptake %
Late semi-stupor	.. 23 Oct.	36	29 Oct.	33	22 Nov.	41
Hypomanic ..	.. 24	51*	30	40	23	40
Manic	.. 25	33	31	42	24	44
Manic	.. 26	30	1 Nov.	32	25	37
Transitional ..	.. 27	35	20	33		
Depressive stupor	.. 28	36	21	40		

* Two-hour reading; see text.

restless and escaped from the hospital. The result is, therefore, not fully comparable with all the others in environmental circumstances. Bearing in mind the absence of dietary control we may say that the other results agree fairly well with one another and show no consistent change between stupor and the height of manic activity, though there is perhaps a suggestion that activity is greater at the onset of manic phase than at its end. If there is a change in thyroid activity with change in mental state, it must be small and of an altogether different order from the change to myxoedema or hyperthyroidism. The manic, like the anxious person, may be expected to give an essentially normal radio-iodine uptake.

DISCUSSION

Although there have been many studies of thyroid gland function in mental illness, the consensus of opinion is that it is normal in the functional psychoses (Bowman *et al.*, 1950; Altschule, 1953), and the present results agree with this. Likewise, the therapeutic use of thyroid gland extracts has proved disappointing except in the uncommon case of periodic catatonic schizophrenia, where it may produce symptomatic cure (Gjessing, 1938), and thyroxine or tri-iodothyronine are equally effective (Gornall *et al.*, 1952). Periodic catatonia is one of the conditions where chlorpromazine also produces symptomatic cure (Kaiser, 1954; Labhardt, 1954; L. Gjessing, personal communication; Crammer, 1957). It is evident from our results, which agree with those recently reported by Reichlin *et al.* (1959), and Newman and Fish (1958), using different methods, that chlorpromazine has no particular stimulant effect on thyroid function in a daily dose usually considered therapeutically effective. In consequence it is likely that in the periodic catatonia patient it acts directly on brain metabolism, and not unlikely that thyroxine also has a direct central pharmacological effect rather than working therapeutically through peripheral metabolic action.

The variability of iodine uptake by the thyroid of the same individual on different days under seemingly standard conditions has been noted by all workers who have made serial determinations with I^{131} or I^{132} . Francois *et al.* (1958), using I^{132} on 23 normal men obtained values ranging from 20 to 31 per cent., and 30 to 43 per cent., and showed that these were quite outside experimental error and must be a sign of some physiological change. Earlier, Hare and Haigh (1955), using I^{131} in both normals and psychotics, attempted to define the cause of the variation and were left with the suspicion that a rise might sometimes be due to a period of heightened alertness to environment, as in a patient's pleasurable awareness of unusual surroundings on a motor-coach outing. The single high reading of 50 per cent. in our cyclical patient is consistent with this. In animal work Harris (1957) has been able to demonstrate changes in the rate of thyroid secretion in response to brief environmental

changes of emotional significance. It is possible, then, that in man also the thyroid is responsive to significant external events, whereas it is unaffected by those internal events which manifest themselves as psychiatric syndromes, for in anxiety states, manic excitement, stupor, active paranoid schizophrenia, and so on, it appears to continue normal function.

However this may be, until the variability in thyroid uptake readings can be understood and controlled, attempts to correlate mental change with change in iodine uptake ("ring count"), for instance during insulin coma treatment (Batt *et al.*, 1957), are bound to be invalid. Only lack of change can at present be considered significant.

SUMMARY

1. Thyroid function has been measured by the use of a short-life iodine isotope, which allows daily repetition of observations, in a group of 20 chronically psychotic men, and in a man with a 6-day manic-depressive cycle.

2. By this test thyroid function was essentially normal in all.

3. In any individual most of the measurements agreed well, but there were always a few which deviated widely. This has been noted also by others and its explanation is unknown. It invalidates attempts to relate changes in iodine uptake to changes in mental state.

4. Administration of chlorpromazine (300 mg. daily) for at least three months produced a very small increase in thyroid function (radio-iodine uptake), which failed to reach statistical significance unless it was assumed to be superimposed on a mild, possibly seasonal, functional depression of activity.

5. In the cyclical patient no significant difference was found in thyroid activity between manic and stuporose days.

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PROBLEM-SOLVING DEFICITS FOLLOWING WOUNDS OF THE BRAIN*

By

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THIS paper is based upon an investigation that I carried out some years ago into the intellectual changes that resulted in a group of 71 men following wounds of the brain (Jarvie, 1954). These men had been wounded, by high-velocity missiles, during the late War or in the Korean Campaign, and damage to most areas of the brain were represented in the series; the wounds showed all degrees of severity from small areas of cortical contusion up to extensive destruction within the hemispheres.

A number of mental tests were used in investigating the intellectual changes. These tests were: Raven's Progressive Matrices, 1938, the Hartford Retreat Test (H.R.T.), and an Army selection test—the Dominoes Test.

These tests are hardly complete measures of the many complex functions that go to make up human intelligence; but they undoubtedly measure something. An examination of the tests seemed to indicate that, whatever the media might be in which the tests are set, each test measures the same thing, that is, the subject's capacity to solve problems. It became the main aim of the investigation to identify those cases in which problem-solving deficits would be clearly demonstrated, and to study the kinds of brain injury that were responsible.

In 32 of the 71 cases information was obtained, from the man's service record, about his intellectual capacity before he was wounded. In most of the 32 cases this consisted of his actual score on either the Matrices or the Dominoes Test; but in a few cases, only the man's Selection Grade (S.G.)—comparable to the percentile grade on the Matrices—was available. Where there was no information about the man's pre-wounding intellectual capacity reliance had to be placed on the level which he was able to reach on a vocabulary test; in this instance the Hartford Retreat Vocabulary (H.R.V.).

In only 7 of the 71 cases was it possible to demonstrate a substantial deficit in the capacity to solve problems. There were undoubtedly other cases in the series in which less significant deficits in problem-solving were present, but, for a number of reasons, it was impossible to be sure about these. I have not time to discuss these reasons in detail, but the two principal ones were:

1. The unreliability of the vocabulary level as an accurate indicator of the man's pre-wounding intellectual capacity. When the H.R.V. and the problem-solving tests were given to a group of normal controls it was found that the relation between the vocabulary level, and the scores on the problem-solving tests, could be quite discrepant except where the vocabulary score was high.

* Read at the Annual Conference of the British Psychological Society, Hull, April 1960.

2. Other intellectual changes resulting from the brain injury, such as dyslexia and dyscalculia, interfered with the man's ability to do the tests and made interpretation of the results difficult.

TEST RESULTS

The results of the mental testing are shown in Table I.

The age is the man's age when tested by me.

The maximum possible score on the H.R.V. is 40. In my normal control group the median score was 26.

The maximum possible score on the Matrices is 60, and Raven's median for this test is 44 (Raven, 1950). The median in my control group of 50 normal subjects was 43.

The maximum possible score on the H.R.T. is 20. The median score in my normal control group was 14.

The 15 subjects in the normal control group who produced a vocabulary score of 32 or over (the lowest vocabulary score in the brain wound cases, except Case 56) showed a range of score on the Matrices of 43 to 56 (median 51); and on the H.R.T. of 10 to 20 (median 17).

The Dominoes Test was only made available to me after the investigation began and for this reason it was not used in testing the control subjects; this also explains why it was not given in Cases 5 and 12, the men having been discharged from hospital and it not being possible to recall them. The maximum possible score on the Dominoes Test is 48; the median 28.

I trust you will agree that in these 7 cases deficits have been convincingly demonstrated, on each problem-solving test used, even when allowing, in the older men, for any slight falling off in test performance due to the natural processes of ageing.

TABLE I

Case	Age	H.R.V.	Matrices	H.R.T.	Dominoes	Pre-Wounding Level
1	24	33	34	7	20	S.G. II—Matrices 48
5	37	32	26	3	—	No information
8	38	34	15	2	18	No information
12	31	35	35	11	—	Army first-class certificate of education
17	37	39	35	10	23	School certificate with 6 passes—qualified sanitary inspector
31	40	35	33	10	22	No information
56	19	26	21	6	19	S.G. III plus—Dominoes 29

ANATOMICAL FINDINGS

In considering these brain wound cases anatomically it should be remembered that the amount of cerebral cortex put directly out of action is usually relatively small, and that damage to the fibre tracts running within the white matter is the main consequence of the penetration of the brain by the missile.

In 3 of the 7 cases the white fibre tracts were disrupted by the passage of the missile completely through the brain—this is illustrated by Case 8 (Fig. 1).

In the other 4 cases the white fibre tracts were disrupted by the deep penetration of the missile into the posterior frontal or anterior parietal region,

CASE 8

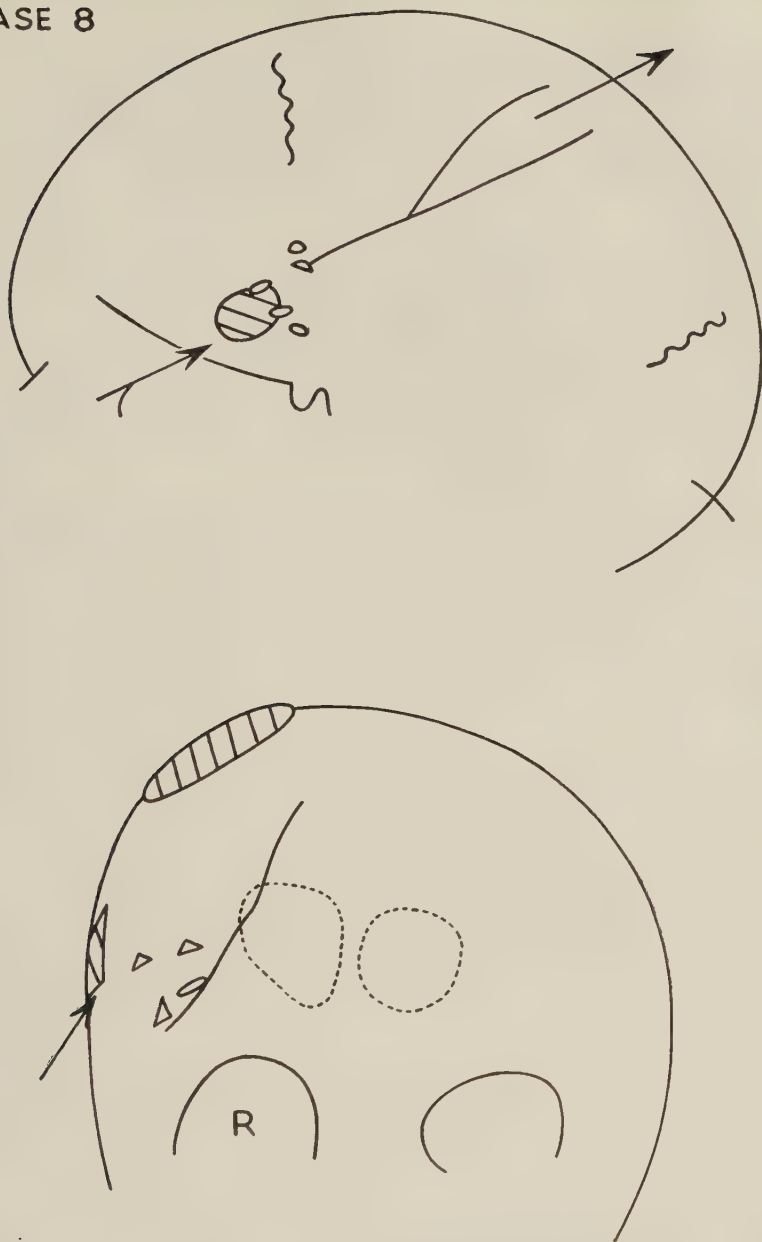


FIG. 1.—Tracings of skull radiographs in Case 8. Self-inflicted injury. Bullet entering right frontal lobe 3 cm. behind right eyebrow and passing through-and-through: exit right parietal region.

areas where the fibre tracts are maximally concentrated—this is illustrated by Case 17 (Fig. 2).

It should be noted that in 5 of the 7 cases, as far as one could tell, the damage was restricted to one hemisphere.

Although the effects of injury to the cerebral cortex at the points of entry and exit of the missile cannot be entirely excluded it would seem reasonable

CASE 17

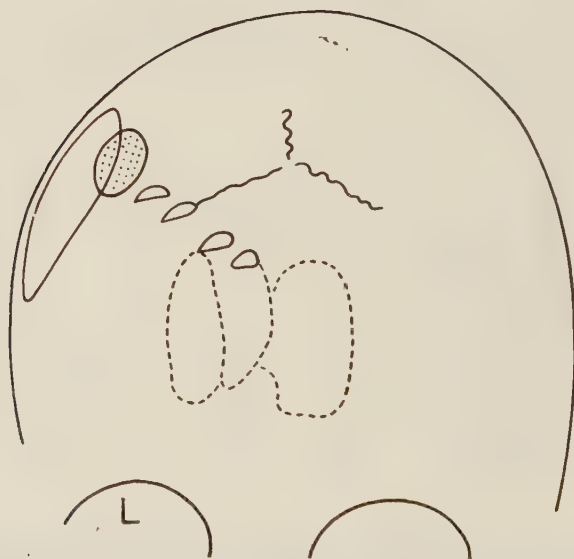
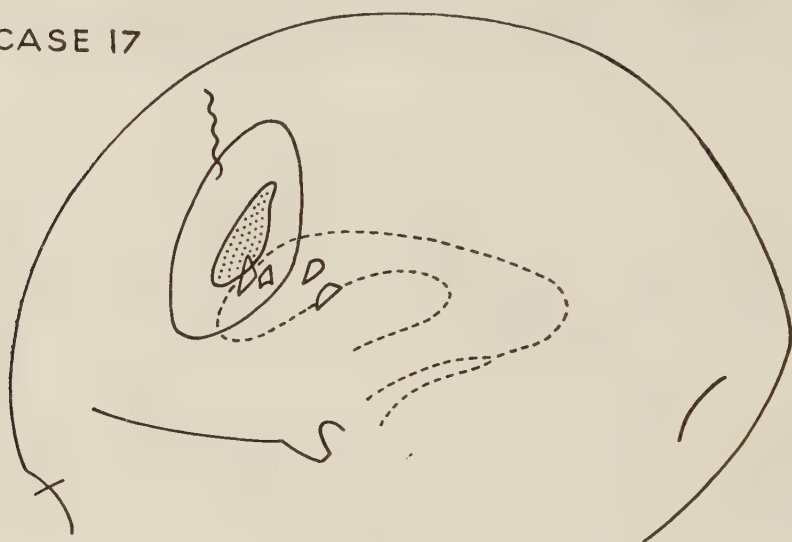


FIG. 2.—Tracings of pre-operative skull radiographs in Case 17. Bone fragments driven into the posterior part of the left frontal lobe to a depth of 5 cm.

to conclude that the diminished capacity for problem-solving shown by these men results from the isolation of different areas of the cerebral cortex from each other rather than being due to damage to limited areas of cortex specifically concerned with this kind of intellectual function.

COMMENT

It is a far cry from the rat to man, but it is interesting to speculate to what extent these observations from human material can be compared with the experiments of Lashley (1929) on the effect of cerebral lesions on maze learning in the rat. In the rat there is progressive difficulty in forming maze habits as the size of the lesion, generally irrespective of its location, increases; with a given extent of lesion, although the rat can learn simple mazes, it finds it less easy to learn complex ones.

The wounded man can still solve problems, otherwise they would not have scored at all on the problem-solving tests; it is only when they work through the tests, and the problems become more difficult, that they begin to fail. In the rat the lesions were grossly ablated areas of brain tissue, whereas, in the wounded men, I have described the lesions rather in terms of the isolation of areas of cerebral cortex by the severance of the connexions between them; functionally, however, the end results in the two instances are probably not dissimilar.

To Lashley, maze learning in the rat is a manifestation of a general intellectual capacity, and this capacity is a dynamic function of the whole cortex and not specifically related to any part of it. Presumably this capacity is equivalent to Spearman's general intellectual factor *g* (Spearman, 1923). The tests that were used in examining the wounded men, in particular the Matrices and Dominoes Test, are certainly *g* saturated. Does this mean that we can conclude from the observations described here that the general intellectual factor is also a homogeneous function of the human cerebral cortex; much indeed as Spearman himself conceived it to be?

One further observation from these cases requires consideration. Although deficits in problem-solving were shown to be present, other kinds of intellectual activity remained, apparently, intact. Verbal ability, for example, was well preserved in these cases. This was impressively demonstrated by Case 8. This man was not only able to score 34 on the Hartford Retreat Vocabulary, but following his injury he remained a prolific reader and kept a supply of the latest books beside his bed. When employed in a practical situation, however, he was incapable of performing effectively any kind of constructive task. His performance on the problem-solving tests was the poorest in the group of 7 cases.

In this man the preservation of verbal ability was not limited to the acquisition, remembering and reproduction of verbal material, but he was also capable of organizing verbal material satisfactorily. He wrote, at my request, a review of a book that he had just read—and a reasonably competent review at that, and composed a readable article for the hospital newspaper—all this with the white matter of one hemisphere disrupted but, needless to say, his dominant hemisphere intact. It would seem that, in so far as this kind of intellectual function is concerned, we must still continue to think of it in terms of localization.

ACKNOWLEDGMENT

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PHOBIA OF OUTER SPACE

By

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THE manifest contents of most phobias concern dangers coming from the environment. It is the degree of those neurotic fears rather than their objects which makes them appear unrealistic. Fears of dangers coming from outside the environment in which the patient lives, such as fear of cosmic happenings, have usually been found to be associated with schizophrenia. Recently the knowledge of our physical environment and the scope of its exploration have been undergoing fundamental changes. This has been reflected in the symptomatology of phobias. The following four patients seen in the psychiatric out-patient department of the United Sheffield Hospitals during the last eighteen months illustrate how a change in the popular concept of physical reality can produce a new type of neurotic fear. The first case is given in greater detail than the others, because the patient's power of verbalization was above average.

Case 1

This patient was a tall burly man of 33 years of age, who was first seen in September, 1957. He was a married schoolmaster with an 8-year-old daughter, and had lost a baby 3 years previously with pneumonia. This had, for a time, intensified his symptoms. He was said to be conscientious and good at his work although showing resentment easily during frustrations with his colleagues. He lived in hilly country just outside Sheffield which made his fears more disabling in his daily routine. His general practitioner referred him with "a type of agoraphobia" from which he had suffered on and off for 4 years. He was said to get sweating and nausea with views and open spaces. At the first interview he said "it first happened on Dartmoor, we were on a tor: you are there surrounded by masses of space. You seem unprotected and very vulnerable". He felt much worse at work (at school on top of a hill) and when travelling downhill to his home.

Over the next 5 months his condition worsened. He felt unsafe "because the earth is a ball spinning round and I am on it". Occasionally the horizon seemed to tilt and if he looked at a picture he felt it was about to turn over. He became completely incapacitated and had to be admitted to hospital with the fear "of going to disappear into outer space". He felt that his feet were on the ground and that the sky was above and he had to keep reminding himself that the force of gravity was keeping him down—"otherwise I would float into space". (At this stage he blamed his illness on his resentment of changes at work, and what he described as his professional pushing around.) Because of depression he had a short course of E.C.T. which left his fears unchanged. Phrases which commonly occurred included: "It's space that's getting me—the curvature of the globe makes everything insecure". "We are surrounded by a hostile envelopment—if I think about it I want to run for cover. I feel more vulnerable stood still than walking. The globe is a globe and I think of the underneath as well." At this stage he went through a particularly distressing time due to daily reports about the Trans-antarctic Expedition (as did Case 2). He would ask "can you imagine you are walking on something unstable" and he would talk of "taking cover from all the space around". His home was described as "a little small house on the globe and all the space above—and that is insecure". If he went outside and saw other people he would say, "do these other people realize what danger they're in on this spinning ball we call a globe?" His fear was summed up by himself as follows: "Primitive man had a fear of the sun and the moon and the stars, and I am the same." The fear on hillsides was due to the danger of "slipping off and floating off into space". Mild earth tremors in East Derbyshire during late 1957 made him afraid of the earth's crust crumbling. His fears were made worse by the setting sun "because it accentuates heights" and "it is like a ball of fire". He was afraid of travelling in certain parts of the city: "it's the chimneys—they emphasize heights". Snow falling at this time of the year made him afraid because of the danger of it upsetting the balance of the earth (Case 2 was afraid of chimneys, oil drilling and coal mining). At a later stage, when attending as an out-patient,

he described his journeys to the hospital "as good practice through the terrible chimney infested regions". From time to time he described his feelings in directional terms, e.g. "getting a bit of the vertical" or "I sometimes get the other space as well—the horizontal aspect—just space rather than ascension".

This patient has been subject to neurotic disorders since early childhood; he remembered that before he was five his mother always made his nerves bad before they went to town. She would "whittle" (worry) him about washing and keeping tidy. He said it used to get on his nerves and he could feel it inside, and that he had had these feelings all his life. It depended on his being in good condition whether he noticed it or not. His mother was a "whittler" (worrier) and he thinks he must have got it from her. He also remembers that his father would not go near aerodromes or aeroplanes—feeling that he had a fear of "the flying part". As a child he was always travel sick on tramcars and particularly in those parts of the city where there were a lot of chimneys. He also showed obsessional features in childhood, worrying if he had done things correctly and "I used to go over things unnecessarily".

He received in-patient psychotherapy of a supportive and abreactive nature for 2 months. This was in sessions of about 40 minutes 4 times a week. During this time he was urged to make increasingly prolonged journeys (at first with a nurse). After his discharge from hospital he felt unable to return to work "because the long journey allows some of these fears to come back". He was seen as an out-patient twice a week for the next 2 months and improved sufficiently to return to work, although he experienced considerable anxiety on some journeys with "the space whipping back" which he thought was made worse by getting tired at work. He was soon able to increase his activities and he regarded himself as having made tremendous progress when he refereed football matches on winter afternoons in spite of the setting sun. In the next 6 months he started driving his car into the Peak District and later to the seaside, which had been out of the question for the previous year. It is now 2 years since he was first seen as an out-patient and his only complaint is the "space feelings sometimes whip back for a second or two when I am overtired".

Now when he looks back at his illness he thinks it was brought on by unfair conditions of work, i.e. he was doing extra work without extra remuneration. During the war he was a navigator in the R.A.F. but does not relate this to his illness. He remembers that when the latter started he was a geography master using a globe and looking at it as though from outer space. He thought his illness was also related to drawing diagrams of the earth in space for the schoolchildren. He said that he had never had trouble with his ears or sense of balance and had passed an aircrew medical examination for this.

Case 2

The second patient was a successful business man of 40, with feelings of insecurity going back to childhood and space feelings for almost 20 years. He was married with 2 children and had been in satisfactory employment with the same firm since leaving the Army in 1946. He had been a popular colleague and had worked his way up to a directorship of a small company. The fears first became troublesome in 1940 immediately after the "blitz" on Sheffield (1940), where he was stationed on Army Service. He had recently met his future wife and they married a few months later. His first complaints were of feeling frightened when he was out, when he would break out into a sweat, having to run to wherever he was going. He then developed a fear of the world spinning round which was accentuated in open spaces. The fear was worse on route marches. He went sick with these fears at the beginning of 1943 and he was seen once by a psychiatrist.

The patient became worse over the next few months which was towards the end of 1941, and then he showed the following features. He was afraid of heights and of going upstairs, because it made him feel that the world was round. He used to get "tied up" in a tramcar going one way, and the earth spinning another way, and he could not sort out which way he was actually going in space. It gave him a tense, tight feeling inside. These symptoms improved a little at the time of his marriage early in 1942 but never left him. He also said that he was never happy on walks unless "near woods where there is some protection", and he was also afraid in the open where he "couldn't get into protection quickly". He said that views used to "get hold" of him, giving him a feeling that there was nothing underneath him. Whenever he thought of people moving coal and oil (by mining and drilling) he felt "by God, someone's going to upset the equilibrium of the whole sphere" (c.f. rain and snow, Case 1). He never got over the fact that people are under us walking upside down, and he was upset last winter when listening to broadcasts of the Test Matches played in Australia (c.f. Case 1 and the Transatlantic Expedition).

As a child he remembered looking through his legs and seeing everything upside down, which made him dizzy. The setting sun caused him to work things out, e.g. "am I standing on a slope?" The stars at night caused him to think "let's get inside and get some protection". He said "an expression I use is a feeling of vulnerability (c.f. Case 1)—it's difficult to describe". He said that he used to get a similar sort of feeling under chimneys and mentioned a particularly large chimney in Sheffield which always produced this feeling.

He continued his war service (sergeant R.A.S.C.) in the U.K.—not without difficulty, though he never went sick. He was very grateful when he became a sergeant because "it was easier to work it out to keep near protection". After the war he was relatively well for several

years although never happy in exposed views, and described "thought going through your mind of the distance rain falls—it gets you boggled".

Two years ago his symptoms, which had been present but not troublesome since the war returned with unpleasant intensity, sufficient to place restrictions on his normal activities. He put this down to "emotional strain". He said that he imagined himself in love with the wife of a friend, and at the same time his wife was expecting another baby. As a result he described himself as becoming all upset. At the onset of this exacerbation he went down a coalmine and the cage upset him because he was terrified of lifts and anything he could not control.

At an interview he discussed his space fears saying "there is so much talk (about outer space) these days—it makes you boggle to think about it". "I boggle at the idea of satellites being put up—they are stationary space stations and yet they are going round—I can't sort it out". Ships also make him feel afraid "because of the space above, below, and round you". The thought of flying made him turn over. One of his main worries on becoming a company director was the possibility of having to fly on business trips.

His childhood was described as difficult. His father was initially very well off and lost all his money in the slump, when the patient was 5 years old. He described his father as "a big-head with a heavy hand". There was an undercurrent of tension all the time and his mother had to play the piano in a public house, which he thought was degrading. There were no gross neurotic features during childhood but during group psychotherapy considerable resentment was repeatedly expressed towards his father. He also said that his security came from his mother, who was herself insecure. As he grew up he had feelings of inferiority and self-consciousness. He "always wanted security" and didn't want to carry on with the same quarrels and shortages as in his childhood. He became a meticulous and mildly obsessional person.

Treatment consisted of out-patient group psychotherapy. This was a mixed and closed group of 8 patients for 1½ hours in one session per week for 10 months. At the end of this period he was virtually symptom free, and fears of outer space caused no social disability. Looking back he could not account for his particular fears and regarded it as "a morbid interest since 1940". It was not related to his job or other interests. He remembered that he had complained of singing noises in his ears since his Army days and had an examination from the medical officer for this. He occasionally suffered from wax in his right ear. Otological examination (including tests of vestibular function) revealed no abnormality. He considered that group psychotherapy was of considerable help to him.

Case 3

The third patient was referred by her general practitioner during the summer of 1959, "because of headaches since the age of 3". The patient was an attractive, well-developed girl of sixteen who felt unsettled at work. She described her headaches as being due to "migraine like father had". They were not preceded by any prodromata, were right sided and lasted all day. They included the right side of the face and neck and occurred 2 to 7 times a week. She said she had always been anxious, with a fear of the dark, and of something going to happen—for example developing a growth in her head.

At home she had to keep tidying her things, and rearranging the contents of her drawers. At work in a gown warehouse she had to re-check piles of dresses 2 or 3 times, and to go round picking bits of tissue paper off the floor. It was only on specific questioning about space fears that she described them. She said that she had never mentioned them to anyone before. Fears about the earth had existed for about 11 months. She felt that it was suspended in space and was unstable, and that it might collide with another planet. "We are suspended in air and I wonder how safe we are. It is queer to think we are turning round and round and turning upside down." Space fiction and television programmes about outer space interested her particularly, and she denied being afraid of the prospect of making journeys into outer space. She felt more space conscious as the sun was setting. She showed no agoraphobia, but was afraid of heights.

Her childhood was unhappy. Her father suffered from migraine and drinking a lot. He was always hitting both the patient and her mother. She was a nail biter as a child. Considerable upset was caused in 1957 by the death of the grandmother who had brought her up. The re-marriage of her mother 12 months later made her feel more settled. Headaches had occurred first at the age of 3 when her father returned from war service abroad. She remembered him as being cruel and never nice to her, and always unpleasant when drunk. She was never fond of him, and as a child was always afraid of something going to happen (such as Dad coming home drunk and beating them up). Recently her headaches were common on Tuesdays and Thursdays when she had to face a particular typing teacher at work—whom she described as ill-tempered. The lessons were sometimes missed because of this. At the time of the completion of this paper she was being treated as an out-patient on supportive lines. Otological investigation revealed no abnormality to cause her symptoms.

Case 4

The fourth patient was a married woman of 29, with 2 children. She was first seen one week after the previous case, and did not mention space fears until asked about them. The general practitioner referred her because of chronic anxiety and frigidity. Her main worry

was that she had been anxious since adolescence, and felt she was now passing this on to her children. She showed obsessional personality features and she used to re-check the gas taps in the house repeatedly. She mentioned pains in the stomach which she had always thought of as cancer, and pains in the neck which she had thought to be due to poliomyelitis. Travelling on the roads and in lifts made her afraid. Two children close together (ages 1 year and 2 years) were suggested as a reason for worsening of the symptoms. She said she was afraid of "the universe", getting tense when she thought of being upside down and spinning round. She had to listen to space programmes on television, "but it's a nuisance when you are interested in things and they frighten you". "The world is unstable and may collide and blow up. The world is more unstable when I feel unstable. Other planets and stars collide and explode. They say the sun will blow up one day and it's rather a frightening thought." She is also claustrophobic, afraid of heights, cliffs, and falling off piers. These fears have worried her since "I knew the world was not the be all and end all". She also said she was afraid to sleep in a strange room because of waking up to find the walls and the floor in a different place. Like Case 2 she could not stand seeing a picture upside down. She felt that there were peculiar things happening in the universe, e.g. there was too much radiation, and there might suddenly be insufficient air. When thinking of the universe she said "the earth isn't there and the sky there—but it's spinning round all the time—you get confused—everyone has to bring themselves down to earth occasionally". She became worried "about all the collisions there might be up in outer space because of all this indiscriminate sending up of satellites". She felt, "there is no planning and it might affect the natural order of things".

This patient has been seen regularly as an out-patient and has recently been fitted into a group for psychotherapy.

DISCUSSION

All four cases showed the typical clinical features of neurotic anxiety with a variety of phobias related to space. Fear of disturbance of equilibrium was present in each case. There was no indication of vestibular dysfunction in any of them. In all four cases there was a history of neurotic anxiety in childhood, which was clearly related to a sense of insecurity; in three patients it appeared to have been created by unhappy relationship to the parents, and in one to excessive standards set by an over-solicitous mother. All four patients showed marked obsessional personality features.

The phobic preoccupation with space at first took the form of fear of heights and of agoraphobia. Fear of outer space and of cosmic catastrophes supervened at a later stage. The first two patients had during the war experienced threats coming from distant spaces though not from outer space. In the second case the sphere of danger increased from the range of enemy bombers to the infinity of the universe. All patients experienced anxiety about the security of their attachment to the earth. The first patient in particular expressed doubts about the reliability of his own gravity. All four felt the gravity of the globe and its movements to be precarious. They were preoccupied with fears of the earth deviating from its course and being destroyed in a collision in outer space. Artificial satellites were felt to increase this danger. In all four patients the sight of the setting sun touching the horizon exacerbated the phobia. They were aware that the frightening character of this sight was due to the globe and the sun meeting within the visual field.

The four cases reported here are worthy of interest because they demonstrate the influence of cultural factors on neurotic symptoms. The growing preoccupation with outer space is one of the features of our present civilization. It is not surprising that it should enter into the manifestations of certain neurotic symptoms. The same happened when bacteria became generally known. Possibly, with bacteria having lost some of their terrors, bacteriophobia will become less frequent and other phobias, such as the one described here, will take its place. It appears that the contents of phobias are more liable to reflect common anxieties than are other neurotic symptoms, such as those typical of hysteria which tend to express problems and conflicts in more individual terms.

The number of cases reported is too small to permit of generalizations. However, it is of interest that all of them showed marked obsessional personality features. It would not be surprising if space phobia should regularly be found to be associated with that type of personality. Obsessional personalities tend to be preoccupied with spatial relationships and are apprehensive of changes in those relationships, especially if they cannot control them. The concept of the infinite universe implies infinite uncertainties which the obsessional might find it difficult to tolerate. Schilder*, who discussed the significance of space in neurotic symptoms, noted that the obsessional neurotic tended to limit and, if possible, to contract his spatial environment. If this should be so, the present-day emphasis on its limitless expanse could create anxiety in those patients. Schilder's observation is in need of further study. In his view, the abnormal space experiences of the neurotic symbolize their inner uncertainty concerning their actions. Space phobia, with the picture of the globe leaving its course and colliding with other bodies, can be regarded as a projection, in terms of the space age, of anxiety arising from unconscious conflicts. The question why these anxieties should take this particular form in some individuals, cannot be answered on the basis of a purely clinical investigation. Possibly, the use of the psychoanalytic method may throw light on this problem.

SUMMARY

The symptom of space phobia has been described in four patients. Its relationship to the obsessional personality type has been discussed. It illustrates the influence of cultural factors on neurotic symptom patterns.

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* Schilder, P., *Internat. J. Psychoan.*, 1933, **13**, 274.

THE COMPLEXITY OF MOTIVATIONS TO SUICIDAL ATTEMPTS*

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ATTEMPTED suicide is a non-fatal act of self-damage carried out with the conscious intention of self-destruction. This is the only definition about which clinicians can be expected to agree. Attempted suicide was, until recently, regarded only as an abortive or unsuccessful suicide. Consequently, it was studied purely retrospectively, which is appropriate for events which mark the ultimate end of an individual. Motives, methods, clinical diagnosis, social factors leading to the suicidal attempts were examined and the available figures were interpreted in the same way as the suicide figures. In the published studies, the number of attempted suicides used to be smaller or did not greatly exceed those of suicides occurring in the same population. It is not surprising that non-medical research workers should have accepted them as reliable approximations to the true incidence of suicidal attempts, but many psychiatrists have done the same, which illustrates the deceptive magic of figures.

THE INCIDENCE OF SUICIDAL ATTEMPTS

No psychiatrist had until recently tried to investigate the incidence of suicidal attempts. Another equally surprising gap in the knowledge of attempted suicides was the lack of follow-up studies. Apart from two notable exceptions, no research into the fate of people who had made suicidal attempts had been carried out. The two exceptions were: first, Stelzner's follow-up study of 200 cases admitted to the Berlin Psychiatric Klinik, published in 1906. The purpose of that study was to compare the natural history of psychoses in the course of which attempted suicides had occurred, with that of comparable psychoses without this complication. It was found that the two groups did not differ with regard to their natural history. The authoress did not even comment on the very small number of patients who had committed suicide during the period under survey. The second catamnestic study was published in 1945 by Dahlgren of Malmö, who was interested in the same problem as Stelzner. Fourteen of his 237 patients had killed themselves within four years following the suicidal attempts which had led to their admission. Dahlgren found no difference in the incidence of final suicides among psychotics, neurotics and personality disorders. He regarded his series as representative of attempted suicides although their number had been smaller than that of the suicides which had occurred at Malmö during the same period. The authors of these and other studies looked at suicidal attempts as a kind of suicide. Even today the word suicide is often used in the literature for both the fatal and the non-fatal suicidal act, the implication being that the latter is just a minor version of the former. This is true, but attempted suicide has many other equally important implications. Attempted suicide undoubtedly happens much more often than suicide. Precise figures will,

* From a Maudsley Bequest Lecture, delivered on February 8, 1960.

for obvious reasons, never be available, but it is possible to make certain basic estimates about the ratio of attempted suicides to suicides. In a British city of about half a million, such as Edinburgh or Sheffield, the number of suicides will vary between about 50 and 100 per annum. Every single psychiatrist working in such a community sees at least that number of attempted suicides, probably more. It has been estimated that the number of attempted suicides is about 6 to 7 times as high as that of the suicides, which would mean about 5,000 attempted suicides per year in Metropolitan London, surely a very conservative figure. Follow-up studies of several samples of suicidal attempts (Stengel and Cook) showed that only few of those people, 1 to 5 per cent., killed themselves within the following 5 to 10 years. Although none of those samples could be regarded as representative—it is doubtful whether such a sample is obtainable—it is of interest that they differed from the typical suicide samples with regard to age and sex distribution. The peak of the attempted suicides was in middle age and females were in the majority, which is at variance with the suicides, which have a later peak and a male majority. At any rate, in the light of follow-up studies it can be stated that suicides and attempted suicides present two different populations, of which only two characteristics are known for certain.

- (1) The former are all dead, while the large majority of the latter stay alive.
- (2) There are many more of the latter than of the former. Those two populations overlap, a small number of the one, i.e. of the attempted suicide group, entering into the other, i.e. the suicide group, in the course of time. The thesis of the two different, though overlapping populations is further supported by the fact that according to the information available only a minority of those who commit suicide have attempted suicide before. Therefore, if one treats those who commit suicidal acts, i.e. suicide and suicidal attempts, as one population, it is a population consisting largely of attempted suicides with a small minority of suicides. The vast majority of people who have made suicidal attempts continue to be the doctor's concern. Follow-up studies carried out in Switzerland by Schneider confirmed these findings. However, a note of warning is called for. Small though the proportion of those who, having attempted suicide, finally kill themselves may be, it is, of course, much higher than the proportion of suicides occurring among the general population. People who have attempted suicide are, in fact, a group with an excessive suicidal risk.

There has been some controversy as to whether or not the groups of cases available for study should be subjected to a statistical analysis, although they are not representative samples. A statistical analysis can be very misleading if applied to unsuitable material. The following consideration illustrates this pitfall. Suicide has been shown to be relatively more common in the upper than in the lower social classes, at least in Western society. However, among suicidal attempts accessible to analysis the upper classes were invariably under-represented. To the statistician this may mean that they are less prone to suicidal attempts and more to suicide than the others. The clinician would reject such a conclusion. The apparent difference is probably due to the fact that while admission to the coroner's mortuary is entirely unselective, the same does not apply to public hospital departments to which people who have made suicidal attempts are admitted. To subject such figures to a statistical analysis is apt to bestow on them the undeserved dignity of scientific statements.

THE APPEAL FUNCTION OF SUICIDAL ACTS

The behaviour patterns of attempted suicides, the individual's relationship to, and his communications with other people immediately before, during

and after the attempt, have been closely studied (Stengel and Cook). Warning of the impending suicidal act were found to be the rule rather than the exception. Most people who attempt, and many who commit suicide, remain within the social field, i.e. near others. The immediate and lasting repercussions of the suicidal act on the human environment were examined in a large number of cases. A great variety of reactions to it were observed. In many instances they transformed the patient's life situation permanently or transitorily. The suicidal attempt acted as an alarm signal and as an appeal to the human environment, although it was not as a rule consciously meant to do so by the person committing the act. However, regular and predictable consequences of a voluntary act such as attempted suicide are apt to play a part in its motivations, i.e. the urges and sentiments which set it into motion. This is why it is essential for the understanding of a purposive action to consider its various predictable effects. Nobody doubts that the wish to destroy oneself and to die, which is the effect of a minority of suicidal acts, enters into their motivations. The large majority of suicidal acts, i.e. the so-called suicidal attempts, have alternative consequences which are broadly predictable. Psychologically speaking, it is not quite correct to say that the only effect of suicide is death. It usually has considerable psychological consequences beyond this effect, because it calls forth grief reactions and guilt feelings among those close to the person who has killed himself. It often leads to a belated upsurge of affection, in short many of the things happen which some of the people contemplating suicide envisage in their phantasies, and sometimes ask for in their suicide notes. The difference between those reactions to suicide on the part of fellow-men and those to attempted suicide is that in the case of the former they are posthumous, while in the case of the latter they can reach the person who committed the suicidal act. The appeal function of the suicidal act was by some critics understood invariably to imply a conscious intentional appeal. This is true only for a minority of cases where side by side with the self-destructive intent the alternative of the appeal effect in case of survival was contemplated. One of the critics argued that if suicidal acts had an appeal function, there ought to be far fewer of them in our civilization because society was so prosperous today. Such arguments are based on a misconception. The suicidal attempt acts as an alarm signal and as an inarticulate and unspecified appeal for help in distress. Everyday observation shows that there is nothing like a suicidal attempt to call forth helpful reactions from the environment. This reaction may sometimes consist in protecting the individual against himself.

The concept of the appeal function of the suicidal act has a certain ambiguity which reflects the complexities and ambiguities of suicidal motivations. Nobody can deny that a suicidal attempt acts as an appeal for help, but the same is true of an accident, and indeed of illness. The difference between the psychological effects of those afflictions and of those of a suicidal attempt springs from the fact that the latter is a purposive act which in case of survival can be expected to have this effect. This is why the possibility of the appeal function playing a part in the multiple motivations of a suicidal act can never be ruled out even though only a minority of individuals may be conscious of it.

Individuals and society as a whole have often tried to reduce the incidence of suicidal acts by depriving them of their appeal function. There is a belief that suicidal intentions can be countered by apparent indifference or even by threats of punishment, which in the case of a fatal outcome used to consist of public disgrace.

Should suicidal acts, because of their appeal function, be regarded as

hysterical manifestations? This question has been discussed elsewhere (Stengel and Cook). It was pointed out that the appeal effect of an action does not make it hysterical, but that this effect would make it liable to be exploited by hysterics and psychopaths.

THE SUICIDAL ACT AS A GAMBLE

There is a marked similarity between gambling and most suicidal acts. Their outcome usually depends on a variety of unpredictable factors among which the intervention of the environment is important. Only a small minority of suicidal acts are carried out in such a way that there is nothing left to chance. Survival is usually accepted without demur, at least for a time. This is why the suicidal attempt has been likened to an ordeal, i.e. a dangerous trial whose outcome is accepted as the will of God or of Providence (Stengel, 1952). In some cases the suicidal act is reminiscent of "Russian roulette".

It follows that frequently the outcome of a suicidal act, be it death, near death, or only a slight threat to life, also depends on a variety of factors other than the degree of suicidal intention and the method employed. This is why there is so much confusion about serious and non-serious suicidal attempts. Schmidt, O'Neil and Robins called serious those suicidal attempts which either gravely endangered life or had been undertaken with serious intent. It seems preferable to rate suicidal attempts separately for dangerousness and for degree of intent. Frequently those two factors show an inverse quantitative relationship.

Psychiatrists often speak of genuine attempts without defining what they mean. There is a tendency to imply that an attempt undertaken by a person suffering from a psychosis such as endogenous depression or schizophrenia is always genuine however harmless to life, while so-called unsuccessful suicidal attempts undertaken by neurotics or psychopaths tend to be judged non-genuine, though they may be very dangerous. The feebleness of the self-destructive efforts of psychotics has often been excused as being due to their illness, which rendered the patients inefficient. This explanation is unconvincing, because severe psychotic illness is quite compatible with a determined suicidal act which leaves nothing to chance. If one considers that an element of gambling is a common feature of suicidal acts irrespective of diagnosis, one becomes very sceptical of the simple division into the genuine and non-genuine attempts. And yet, this distinction is used by many psychiatrists as the main guide to action and inaction. Not all suicidal attempts require to be treated as equally serious as far as the suicidal risk is concerned, but it would be mistaken to regard even a considerable degree of uncertainty about the outcome of the suicidal act as an indication of a slight or absent risk. If one classes only those suicidal acts as genuine which but for a miracle or an accident or a miscalculation would have been fatal, their number would be extremely small. The fact is that uncertainty of outcome is a feature of the majority of suicidal acts.

Suicidal acts as gambles with life and death deserve special study. The urge to gamble appears to spring from primitive instincts. To test uncertainty, to take risks by facing hazards is one of the tendencies which pervade human behaviour. John Cohen has lately carried out experimental studies into that tendency which he tried to measure. He demonstrated among other things that the urge to take risks increased as the result of alcohol intake. He believes this effect rather than lack of judgment to be responsible for the increased accident proneness of motorists after consumption of even small amounts of alcohol. Cohen's observations link up with the well-known increase of suicide proneness under the

influence of alcohol. They might take us a step further than the conventional explanation that alcohol increases suicide proneness because it makes some people depressed and removes their inhibitions. The study of suicidal acts as risk-taking actions should throw light on some of their most bewildering features, especially those related to the uncertainty of outcome.

MULTIPLICITY AND AMBIGUITY OF MOTIVATIONS

According to the conventional notions of suicide and attempted suicide, everything that does not serve the purpose of self-destruction is a contamination of the behaviour appropriate to suicidal acts. However, in most of those acts certain features which do not originate from the urge to self-destruction can be discerned. This urge is, of course, present in every suicidal act and so is aggression against others, though the latter may not always be conscious. Notwithstanding those tendencies, the suicidal attempt becomes a meaningful event for the survivor and his fellow-men. The recognition of the appeal function and the gamble character as legitimate features of the suicidal act is of practical importance. It means that suicidal acts in whose motivations those features manifestly play a part cannot, because of this, be regarded as harmless or non-genuine.

Human behaviour usually has multiple motivations, not all of them obvious and some antagonistic to each other. People, according to some psychiatrists, either want to die or to live. That most people who commit suicidal acts want to do both at the same time, and that these suicidal acts may also serve as punishment for others, seems difficult to grasp. Yet there is ample evidence that this commonly happens. To divide people who commit suicidal acts into those who want to kill themselves and those who do not, with a sprinkling of those who do not know, is as justified as to divide married people into those who love and those who hate each other, or parents into those who love and those who hate their children. In fact, the main reason why human relations, and psychiatry, are so complicated and confusing, is that most people love and hate, want to die and to live, and to kill and preserve life at the same time. Why should we expect those people who commit suicidal acts to behave as if they knew exactly what they wanted and to act accordingly? Only rarely is human behaviour governed by one tendency only. The outcome of most human actions, especially of most irrational actions such as suicidal acts, depends on the quantitative relationship of conflicting tendencies and on many other factors, some of them unpredictable. Only in a small minority of people who commit suicidal acts is the self-destructive urge so overwhelming that it completely submerges those tendencies which aim at human contact and preservation of life.

Another kind of dangerous simplification of the suicide problem springs from accepting the patients' explanations of their actions at their face value. The patients are not always aware of all the reasons for their conduct or they may not wish to disclose them. Many doctors too readily accept a patient's denial of suicidal intentions which his actions clearly indicate. Such denials are not always conscious lies, but manifest suicidal behaviour is more revealing and a more reliable guide to the truth than the patient's statements. There are many reasons why patients should deny suicidal intentions and why some suicidal attempts are carried out without a clear awareness of self-destructive tendencies.

It may be argued that the introduction of the concepts of the appeal function and of the ordeal character of suicidal acts is unnecessary and has no advantage over the simple statement that most such acts are carried out half-heartedly

and thus reflect the conflict between the destructive and the life preserving tendencies. There is no objection to this formulation, but closer observation of the patients' behaviour reveals the various manifestations of the life preserving tendencies, particularly the contact seeking features so often noticeable in suicidal acts. They can be observed in premeditated and apparently unpremeditated acts, and irrespective of the underlying clinical condition.

Schilder, in his studies of preoccupations with death, pointed out that in trying to understand suicide, it was necessary to consider what he called the ideologies of death. In this lecture a number of aspects concerning suicide and attempted suicide which have so far received little or no attention have been touched upon. In not confining ourselves to the death seeking urge, and in trying to understand those hidden components of suicidal acts which seek for life and human contact, we are doing justice to man's attitudes to death which has always been felt to be the end as well as a new beginning.

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PSYCHOTIC DEPRESSION AND AGE

By

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INTRODUCTION

THE subject of the present communication arose from an incidental observation made during an attempt to establish a Symptom : Sign Inventory for use with all types of mental patients. For some time past all cases diagnosed by psychiatrists as suffering from depression, whether psychotic or neurotic, have been given this inventory. The observation made was that, within the group diagnosed as psychotic, those over 60 years of age did not appear from the inventory to have the same symptoms as those under 60.

PROCEDURE

Subjects

The subjects consisted of three groups of 20 each—neurotic depressives; psychotic depressives of 60 years of age and over; psychotic depressives of under 60 years. The groups contained 5, 5 and 3 men respectively.

Symptom : Sign Inventory

The Inventory consisted of 86 items which were intended to cover all neurotic and functional psychotic groups and to be very close to questions asked by the psychiatrist in his clinical interview. The Inventory has the advantage that every question is asked every patient in the same way. It has the disadvantage that it cannot take a longitudinal history. It was administered orally by different psychologists. A second copy of the Inventory was placed beside the patient so that she could refer to it if she wished. When any doubt existed about the patient's understanding of the question or about the correct classification of the response, illustrations of the behaviour in question were sought. It was explained that it was a standard list of questions that was being asked in order that nothing should be missed and that, in consequence, some of them would not be applicable to the particular patient.

RESULTS

There were 14 items in which the frequency of responses indicating the presence of the symptom or sign was greater by 25 per cent. in the psychotic depressive group under 60 years of age than in the neurotic depressive group. There were no items in which the frequency was greater by 25 per cent. in the neurotic group. These 14 items then constituted a scale for differentiating psychotic from neurotic depressives.

The mean score for psychotic depressives under 60 years was 6.85 (S.D. 2.56) and for neurotic depressives 2.35 (S.D. 2.94). The difference between these means was significant at the .1 per cent. level of confidence (t being 5.17). Of those diagnosed by psychiatrists as psychotic depressives, 18 (or 90 per cent.)

were so diagnosed by the Scale; of those diagnosed by psychiatrists as neurotic depressives 16 (or 80 per cent.) were so diagnosed by the scale.

A psychotic depressive under 60 years of age differs from a neurotic depressive mainly in feeling:

1. An unworthy person in her own eyes; (12-3).
2. A condemned person because of her sins; (12-3).
3. That people are talking about her and criticizing her because of things she has done wrong; (10-1).
4. Afraid to go out alone; (13-4).
5. She has said things that have injured others; (9-2).
6. So "worked-up" that she paces about wringing her hands; (11-4).
7. That she cannot communicate with others because she doesn't seem to be on the same "wave-length"; (10-3).
8. That there is something unusual about her body, like one side being different from the other, or meaning something different; (6-0).
9. That the future is pointless; (12-7).
10. That she might do away with herself because she is no longer able to cope with her difficulties; (8-3).
11. That other people regard her as very odd; (8-3).
12. That she is often bothered with pains over her heart, in her chest or in her back; (8-3).
13. So low in spirits that she just sits for hours on end; (12-7).
14. When she goes to bed that she wouldn't care if she never woke up again; (10-5).

It is noteworthy that the four "guilt" items are all high up on the list, which is arranged in order of discriminatory power. This confirms previous work by Foulds and Caine (1959).

A psychotic depressive over 60 years of age differs from a neurotic depressive mainly in feeling:

1. That the future is pointless; (14-7).
2. When she goes to bed that she wouldn't care if she never woke up again; (12-5).
3. She is troubled by waking in the early hours and being unable to get off to sleep again; (17-10).
4. Unable to understand what she reads, or what people say, as well as she used to do; (13-7).
5. Her hand shakes when she tries to do something; (14-9).
6. She has difficulty in getting off to sleep; (18-13).
7. The simplest task is too much of an effort; (15-10).
8. She has difficulty in keeping her balance; (8-3).
9. Other people regard her as very odd; (8-3).
10. An unworthy person in her own eyes; (8-3).
11. So "worked-up" that she paces about wringing her hands; (9-4).

Here only one "guilt" item appears and that in the lower half.

A psychotic depressive under 60 differs from a psychotic depressive over 60 mainly in feeling:

1. A condemned person because of her sins; (12-5).

2. Less often that her hand shakes when she tries to do something; (7-14).
3. Less often that she is troubled by waking in the early hours and being unable to get off to sleep again; (10-17).
4. Less often that she has difficulty in getting off to sleep; (12-18).
5. Less often that she has difficulty in keeping her balance; (2-8).
6. Afraid of being in a wide-open or an enclosed space; (9-3).
7. She cannot communicate with others because she doesn't seem to be on the same "wave-length"; (10-4).
8. People are talking about her and criticizing her because of things she has done wrong; (10-4).
9. Less often that she suffers from palpitations and breathlessness; (5-10).
10. Her thoughts rush ahead faster than she can express them; (10-5).
11. Afraid to go out alone; (13-8).
12. There is something unusual about her body, like one side being different from the other, or meaning something different; (6-1).
13. She has said things which have injured others; (9-4).

Here three of the four "guilt" items appear.

It may be noted that sleep disturbance, as assessed by the present method, is associated with age rather than psychotic depression. Thus, 50 per cent. of the younger psychotic group and of the neurotic group complain of early waking against 85 per cent. of the older psychotics. The figures for inability to get off to sleep are respectively 60 per cent., 65 per cent. and 90 per cent. and for diurnal variation (better in the evening) 30 per cent., 30 per cent. and 45 per cent.

Taking the same cutting score that gave maximal efficiency of discrimination between the younger psychotics and the neurotics, 13 (or 65 per cent.) of the over 60s were diagnosed by the Inventory as psychotics and 7 (or 35 per cent.) as neurotics.

The distribution for each of the three groups of scores on the 14 items which best differentiated between neurotics and the younger psychotics is shown in Figure 1.

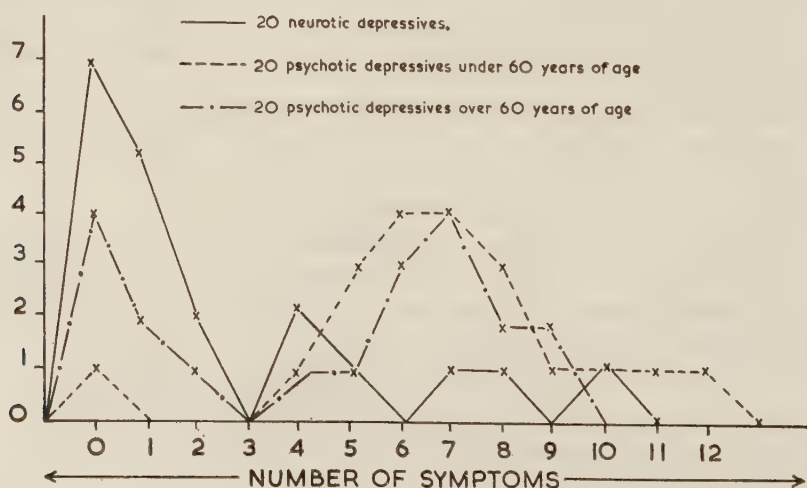


FIG. 1.

CONCLUSIONS

Since the Symptom : Sign Inventory is rather successful in confirming the psychiatric diagnosis in the case of neurotic depressives and of psychotic depressives under 60 years of age, it seems reasonable to conclude that a number of patients over 60 years of age who are diagnosed by psychiatrists as psychotic depressives do not have the same symptomatology as those under 60 years of age who are diagnosed as psychotic. It seems possible from the bimodal curve of the older "psychotic" depressives, that neurotic depression may be rather commoner among the over 60s than is sometimes thought and that this possible fact may be obscured by a tendency for psychiatrists to smuggle in age as a sign of psychosis.

It may be argued that some psychotic depressives are unwilling to reveal their symptoms and that this may account for some at least of the 7 cases in the over 60 group who appeared from the Inventory to be neurotic. It would, of course, be rather curious if this reticence were so much commoner in those over than in those under 60 years of age. One may take the admission of 10 or more symptoms, apart from the 14 "psychotic depressive" items, as suggestive evidence against the "reticence hypothesis". The following are the frequencies in the various groups: psychotic depressives under 60 years, 18 (or 90 per cent.); neurotic depressives, 11 (or 55 per cent.); psychotic depressives over 60 years, who appeared psychotic on the Inventory, 11 (or 85 per cent.); psychotic depressives over 60 years, who appeared neurotic on the Inventory, 5 (or 71 per cent.). From this evidence it would seem unlikely, therefore, that reticence accounts adequately for this group of low scorers (although it almost certainly did for one case).

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CONSCIOUSNESS AND THE HIGHEST CEREBRAL CENTRES, WITH REMARKS ON THE PENFIELD-WALSHE CONTROVERSY

By

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IN deep coma the patient usually lies still, without moving. Why doesn't he move? Many will answer, "Because he is unconscious". This is on the assumption, which seems eminently reasonable; that motor centres are under the control of a higher centre for mind. On voluntary movement, according to this assumption, motor centres receive and obey impulses from the psychic centre. When the psychic centre is paralysed, as in coma, the motor centres lie idle, like men in a factory marking time because the foreman is away and there is no one to tell them what to do.

Hughlings Jackson, a man with an uncanny ability to ferret out the fallacies that may lie concealed behind a façade of logic, referred to this attractively simple explanation as an example of confused thinking. He called it an explanation in form only; in reality it explains nothing.

To show that I am not beating a dead horse, I quote the remark of an eminent neurologist in reference to "psychic equivalents" in epilepsy. (This was in the days before electroencephalography.) He attributed them to "a discharging lesion in psychic centres, just as grand mal is due to a lesion in motor centres".

Jackson rejected the assumption that the highest centres differ from lower centres in constitution, the lower centres being sensory and motor while the highest centres are neither, being concerned with abstract functions only, such as volition and ideation. To him it was unthinkable that as one moves upward in the hierarchy of levels in the nervous system one comes suddenly upon levels with a different *kind* of constitution from those below. He maintained that even the highest cerebral centres are sensorimotor (5), that they co-ordinate impressions and movements of all parts of the body. (By "impressions" he meant those made on receptor organs.)

The problem of the relation of mind and brain has puzzled man since the dawn of philosophy. Lately it has received special attention from Penfield, who has concluded that the centrencephalic system is the highest integrating system, to which the remainder of the brain, even the cerebral cortex, is subordinate. Walshe has challenged this view. I shall try to show that both men are guilty of error. I am well aware that one who steps in between two parties in dispute is likely to be greeted with a shower of brickbats from both sides.

Penfield's papers on the centrencephalic integrating system (CIS) are well known. Stimulation of some parts of the CIS causes alterations in consciousness as well as electrographic changes in both cerebral hemispheres. The CIS has "symmetrical connections with the two hemispheres and with the cerebrospinal axis; connections which make possible integration of the total activity

of the central nervous system" (6). He considers the CIS the abode of Jackson's highest level. He says, "The highest level of integration might be described as that area of the central nervous system in which the final integration of nerve impulses takes place and the efferent stream of voluntary motor impulses is generated" (*ibid.*, page 14). The function of the precentral gyrus is "to transmit, and no doubt to transmute, the impulses which reach it from the central integrating system. This gyrus is a way-station in the stream of volitional impulses" (page 15).

After a detailed consideration of Penfield's position Walshe says (8):

"It seems scarcely credible that within this small and phylogenetically ancient part of the brain such numerous and complex functions could be carried out. How comes it that despite the great development of the cerebral cortex in man, the gamut of physiological and psychological activities characteristic of man should be carried on in these meagre collections of cells in the 'old brain', as Penfield says?"

This is sound criticism indeed.

Walshe's shafts are aimed especially at Penfield's conclusions in respect of the pre- and post-central gyri. He gives (page 525) the following quotation from Penfield:

"Skilled finger movement, like that of a pianist, can only be elicited from the precentral gyrus when it is played upon by well-integrated impulses that come to it in a normal manner from some source within the brain that is functionally higher than the convolution itself. When he begins to play, the pianist does so with both hands and it would seem that only from the upper brain-stem could come the directing impulses that cause the fingers to move across the keyboard . . . Thus, I am suggesting that the master motor area, in the brain of man, may be found at the level of the higher brain-stem where sensory information of finger position is available, where the visual image of the piano is available, where the memory of the music is available, as well as the auditory effect, and where conscious control is exerted upon the mechanisms of movement. Such a master mechanism must contain a sensori-motor complex as well as a complex for conscious thought."

Walshe (page 526) also quotes Penfield's statement that the precentral gyrus "can of itself do nothing. It can serve only as a keyboard upon which the patterned stream of impulses plays" (impulses from the CIS).

Walshe (page 528) makes this comment:

"The student of this hypothesis cannot find it easy to accept the extreme downgrading in the neural hierarchy proposed for the precentral and post-central gyri and for the other primary sensory regions of the cortex. He will remember that the motor cortex has been described by Sherrington as '*par excellence* a synthetic organ for motor acts', and, acting with its fellow, 'an organ for synthesis of movements and postures on a vast scale'. In its new role . . . it has become a way-station only, a passive keyboard played upon by higher levels."

But in objecting to the "downgrading" of the pre- and postcentral gyri to the subordinate status of "way-stations" Walshe exposes himself to criticism. These gyri *are* in fact way-stations, and the motor cortex is indeed a "passive keyboard played upon by higher levels". Penfield erred not in subordinating the motor cortex but in subordinating it to the CIS.

Can Walshe possibly think that the pre- and postcentral gyri, since they are part of the cerebral cortex, belong to the highest level of integration, the highest cerebral centres of Jackson? The proposition that these gyri belong to the *middle* rather than the highest level is the keystone of the Jacksonian arch. It is vital to one of his great achievements, the explanation of the distinction between the grand mal and what he called the epileptiform fit (now called the Jacksonian fit).

Jackson's views on levels in the nervous system may be stated briefly. The number of levels is beyond counting, but for the sake of convenience he divided them into three groups. (For the sake of brevity only the motor half of the nervous system will be considered.) The lowest level consists of the motor nuclei of the cord and the homologous motor nuclei of the cranial nerves. Its centres represent movements most directly and simply. The middle level is in the precentral gyrus. Its centres "re-represent" the movements of the body, and their activation produces relatively complex movements. The highest level is in the frontal lobe anterior to the precentral gyrus, and *its* centres "re-represent" the body in the most complex way of all.

Jackson expressed his views in this matter so often that quotation is hardly necessary. Reference is made to his article on "Relations of Different Divisions of the Central Nervous System to One Another and to Parts of the Body" (Jackson, II, 422) and to the Lumleian Lectures (I, 412). Two quotations will suffice.

After defining the lowest level Jackson proceeded (I, 414): "(2) The middle or second level (its motor province) . . . is composed of centres of the Rolandic region (so-called 'motor region' of the cerebral cortex) . . . It represents complex movements of all parts of the body from eyes to perineum (re-represents). (3) The highest or third level (its motor province) . . . is made up of centres of the prefrontal lobe (highest motor centres), motor division of the 'organ of mind'). It represents most complex movements of all parts of the body from eyes to perineum (re-re-represents)."

Elsewhere Jackson said (II, 83): "The highest motor centres (pre-frontal lobes) co-ordinate movements represented in the middle centres . . . in the sense that the former represent over again in more complex, etc., ways, the movements represented by the latter; just as the latter represent over again and in more complex, etc., ways what the lowest motor centres have represented in less complex ways . . ."

I venture an analogy. The musical instrument, the organ, is supplied with many stops, which modify tone. Thus the oboe stop lends it the quality of an oboe. The organist pulls out the various stops as needed, singly or in combination. There may be a point where he needs a combination of half a dozen stops. In the midst of a piece played in quick tempo he cannot take the time to pull half a dozen stops, and so the organ is provided with couplers that can be set in advance. The organist will set a coupler so that when the time comes he need pull only one stop instead of half a dozen. The precentral gyrus may be said to consist of many such couplers, for a given centre therein will direct a number of centres in the lowest motor level so as to produce a movement of a limb. The highest motor level consists of couplers of the second order, for they couple together various groups of centres in the middle level. Such a system of couplers makes for efficient adaptation.

The matter of unilaterality or bilaterality of representation is important. The precentral gyrus represents one half of the body, while centres in the highest level represent both halves. Most of the things we do involve both halves of

the body. Thus in kicking a football we use not only the right leg but the left as well, plus both arms, the trunk muscles, etc. A "football kicking centre" in the highest level would therefore have to "re-re-represent" the entire body, by way of impulses directed to many centres in both precentral gyri. This explains one of the great differences between the grand mal and the Jacksonian fit. Since the precentral gyrus represents one half of the body, epileptic discharge of a centre therein will cause convulsion that starts unilaterally. Since a centre in the highest level represents both halves of the body, *its* epileptic discharge will produce convulsion of both sides of the body nearly simultaneously (Jackson, I, 156).

Another great difference relates to loss of consciousness. In the Jacksonian fit loss of consciousness occurs late in the seizure, if at all, since the precentral gyrus is not the seat of consciousness. But the highest cerebral centres are the "organ of mind" and so in grand mal consciousness is lost early in the seizure (I, 186).

One of Jackson's shrewdest deductions deals with loss of consciousness in grand mal. Since grand mal is marked by an excess of excitation, one would think that the patient would, if anything, be "hyperconscious". It is a paradox of human nature that the greatest paradoxes (like the greatest lies) are sometimes the hardest to recognize. It took a genius like Jackson to recognize that the unconsciousness of grand mal is a paradox, and his explanation of it is a masterpiece of insight. He said that the highest centres, the organ of mind, cannot function when excitation is unbridled and lawless. The neural substrates of ideas and images are complex, and their useful function presupposes an orderly sequence of excitations correctly timed. He suggested an analogy. If one might suppose a "locomotor centre" in the brain, an epileptic discharge therein would not cause the patient to run fast; on the contrary, it would bring locomotion to a halt, for locomotion demands a harmonious pattern of excitations in correct time and sequence.

Another analogy suggests itself. A legislative assembly does its work with the aid of orderly parliamentary procedure and decorum. The members speak one at a time. If they started to talk and shout all at once, the result would be, not quicker action, but chaos and paralysis of action.

Jackson insisted that the highest cerebral centres are sensorimotor in constitution. He rejected the notion of a centre for mind superior to sensorimotor mechanisms and not itself sensorimotor. Thus he wrote (II, 63):

"A man, physically regarded, is a sensori-motor mechanism. I particularly wish to insist that the highest centres—physical basis of mind or consciousness—have this kind of constitution, that they represent innumerable different impressions and movements of all parts of the body, although very indirectly, as certainly as that the lumbar enlargement represents comparatively few of a limited region of the body nearly directly . . . If the doctrine of evolution be true, all nervous centres must be of sensori-motor constitution. *A priori*, it seems reasonable to suppose that, if the highest centres have the same composition as the lower, being, like the lower, made up of cells and fibres, they have also the same constitution. It would be marvellous if, at a certain level, . . . there were a sudden change into centres of a different *kind* of constitution."

Jackson stressed (II, 440) that the highest centres represent "vast numbers of movements . . . We have (also) to take into account the innumerable combinations into which visual ideas, tactual ideas, the psychical states concomitant with activities of nervous arrangements . . . for manipulatory movements, words and emotions can enter . . ." All these ideas and movements are involved

in consciousness, and the nervous pathways that underlie them are sensori-motor.

By highest centres Jackson of course meant highest anatomically and not morphologically.

To return to Penfield and Walshe, I submit that Penfield is right in "down-grading" the pre- and postcentral gyri to the status of "way-stations". The precentral gyrus is indeed a marvel of complexity, but even so it is no more than a tool for the use of centres above. But these centres above are in the cerebral cortex and not the CIS. As Walshe says, it is inconceivable that the fine activities that constitute mentation should be mediated by structures as primitive as those in the CIS. Functions that involve fine manipulation and fine discrimination, functions like speech and imagery, must be mediated by mechanisms in the neocortex.

Hebb (2), in the discussion that followed Penfield's address at the symposium on "Brain Mechanisms and Consciousness", had this to say: "The answer Dr. Penfield gave to Dr. Magoun, in which he implied that the cerebral cortex and centrencephalic system work hand in hand, removes a misunderstanding of which I was guilty. I thought, to put it in extreme form, that Dr. Penfield meant that conscious processes might continue if all cortex were removed". This comment speaks volumes, even after an allowance for exaggeration. Hebb had thought it conceivable that Penfield might believe that a man with only a CIS and no cortex might yet be capable of "conscious processes".

That the CIS plays a role in consciousness cannot be denied. The work of Morison and Dempsey and Jasper and his associates on the intralaminar system is of phenomenal importance. Thus Hunter and Jasper (3) showed that petit-mal-like seizures can be produced by electrical stimulation in the mesial thalamus. These investigators have disproved one of Jackson's hypotheses, for he suggested that petit mal and grand mal are alike due to a discharge in the highest cerebral centres, the difference being in the intensity of the discharge. Thus he wrote (II, 370, footnote): "*Le petit-mal* passes suddenly into *le grand-mal* when the discharge beginning in some part of the highest centres has become strong enough to overcome the resistance of lower (middle) centres."

What role, then, *does* the CIS play? We may surmise that in some way it maintains alertness. It is related to, if not identical with, the ascending reticular activating system of Magoun. Its role is probably a menial one, like that of the janitors and maintenance men in a university. Without janitors a university would have to shut down. But the essence of a university is in the scientists and professors who work there, not in the janitors who warm up the classrooms and laboratories.

Ferrier (1) said: "The loosening of a pin in a chronometer, it has been said, will derange the whole timekeeping mechanism; but we should not on that account ascribe timekeeping functions to the one part exclusively." Penfield does not ascribe the function of consciousness to the CIS exclusively, but Ferrier's analogy is none the less pertinent. The CIS is probably merely a "pin", albeit indispensable.

Vital as the role of the CIS is, one must not confuse it with that of the neocortex. The two are not in the same class and are not comparable. Penfield (7), in reply to Walshe's criticisms, asks: "Who is to say, at any moment, that brain-stem potentials are more important in a given mental process than those moving through the cortex? Who is to say the reverse?"

I have great respect for Penfield, but submit that this rhetorical question is beside the point. As an example of mental function let us take one used by Penfield, playing the piano. What distinguishes a Paderewski from an ordinary man? Is it the possession of a superior CIS? Not at all. Paderewski was blessed with a superior neocortex.

To sharpen the argument, I will exaggerate the comparison and step it up a notch. The pianist also needs a healthy spinal cord. Paderewski, for all his superior artistic gifts, would have been helpless at the piano had he been stricken with transverse myelitis of the cervical cord. But Penfield does not ask whether, to the pianist, the cortex is more important than the spinal cord, or *vice versa*.

To return to the question put in the first paragraph, why is a man in coma motionless? Since his highest cerebral centres are paralysed, and since these consist of sensory and motor centres, we may say he is motionless from paralysis of the highest motor centres. Jackson put it this way (I, 159):

"To say that a man staggers or lies motionless *because* he has lost consciousness . . . is like saying that a man does not speak *because* he has lost the memory of words, which, at the best, is only repeating in technical terms that he does not speak; it is like saying that a man does not move his arm *because* he has lost volition, which is only repeating in technical terms that he does not move it. Nobody is any the wiser for these 'explanations'; they explain nothing at all; they are attempts to explain physical states by mental states . . .

"Many talk as if a patient could lose consciousness without a loss of use of some parts of the nervous system; or if they admit that there is loss of use of nervous arrangements . . . , the inference from the statement of that admission often is that the nervous arrangements affected did not represent parts of the body, but are centres (that) 'play upon' the lower centres . . . On this view the centres for consciousness are not 'evolved out of', but 'placed upon', lower centres and 'govern' them autocratically . . . On this . . . view, . . . the centres for consciousness are not centres for receiving impressions, and giving out impulses for movements, but centres which 'play upon' lower centres for movements autocratically. On this view, if the centres for consciousness could be sliced away without disturbing the rest of the organism, the physical operations of the body would be positively uninterfered with, though negatively there would be no 'volitional impulses' sent down to put the body in this or that movement . . .

"The view taken in this article is an anatomical one, viz. that the substrata of consciousness are sensori-motor arrangements re-representing all lower centres, and thus representing the whole organism . . . On this hypothesis if they were sliced away there would be loss of innumerable highly complex and most special co-ordinations of the body as a whole . . . ; there would be a degree of paralysis universally distributed . . ."

In the difficult field of the higher functions of the brain Jackson has set an example of lucid and realistic thinking which even today, nearly fifty years after his death, can serve us well.

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ENDOCRINE FACTORS IN THE AETIOLOGY OF MONGOLISM

By

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In the course of the past few decades various controversial theories have been elaborated on the aetiology of mongolism in an attempt to solve the complexity of this interesting clinical entity.

This short study which was undertaken by the writer at Caswell School, Kinston, North Carolina in the spring of 1958, concerns itself primarily with the maternal endocrine dysfunctions as being one of the important factors responsible for the development of mongolism.

A number of Italian (Verga), German (Geyer, Weygant), British (Tredgold) and American (Beidleman, Benda) authorities have expressed the view, based on biochemical, genetic, pathological and clinical studies, that mongolism arises probably from an inborn maternal endocrine disturbance, most likely of a diencephalic origin. It is further held that the inadequacy of hormonal stimulation from that part of the brain in the expectant mother is constitutionally predetermined, having in addition an adverse effect on the dysplastic ovum, and thus creating the necessary conditions for the intra-uterine development of the mongol foetus.

In 1945, Stoeltzer reported three cases in which mothers, prior to the birth of their mongol children, showed severe signs of Graves' disease. The writer has similarly observed a history of serious endocrine disease in six mothers before the birth of their mongol offsprings.

Based on the assumption that one would find a greater incidence of endocrine insufficiency in mothers who had mongol children—study group—than in mothers who had given birth to mentally and physically normal offsprings—control group—the writer has undertaken this investigation establishing his findings on the case histories of 42 mothers of mongol children. It reveals 3 cases of diabetes mellitus, 2 cases of Graves' disease, one of myxoedema and 23 histories of mothers with one or more miscarriages of which 16 preceded and 7 followed the birth of a mongol child.

The control group of 42 mothers of normal offsprings, discloses one case of Graves' disease, one case of diabetes mellitus and 9 cases of one or more miscarriages.

These results thus indicate that the incidence of endocrine dysfunction in mothers of mongol children—14·2 per cent.—surpasses that in mothers of normal offsprings—4·7 per cent.—by almost three to one.

The number of miscarriages were separately investigated, and it was found that the study group revealed two and a half times as many cases as in the control group, namely 23 cases against 9, the ratio being 54·7 per cent. (study group) to 21·4 per cent. (control group).

The result of this small study tends to support the view expressed by the above quoted authorities that the clinical condition of mongolism is traceable to a prenatal endocrine disturbance of a constitutional nature combined with the formation of dysplastic ova and an unhealthy intra-uterine environment.

The study also discloses that the incidence of the birth of a mongol child increases 5 times as rapidly between the ages 25 and 49 as between 15 and 24 (Table II); it is thus advisable to begin laboratory investigations in all expectant mothers who have had a history of major endocrine dysfunction or miscarriages. The measures should include specific hormonal investigations at the time of the first prenatal examination, an X-ray of the foetal skull bones (Benda) and treatment of any hormonal imbalance and nutritional deficiency. The procreation of children during the climacterium should not be encouraged as the risk of the birth of a mongol child during that period is considerably increased (see Table I). Other findings are that the menstrual onset in mothers of mongols

TABLE I

Mongols Born to Mothers at Various Age Groups

Mothers' age groups in years	15·19	20·24	25·29	30·34	35·39	40·44	45·49
No. of mongols born to them	1	9	11	9	11	17	4

TABLE II

Mothers' age groups in years ..	..	15·24	25·49	15·29	30·49
No. of mongols born to them ..	..	10	52	21	41

ranges from 10 to 17 years, the average age being 14·9 years and their mean menopausal age 46·9 years.

The frequent occurrence of psychoneuroses in the histories of mothers of mongol children and those with endocrinopathies points to a psychosomatic involvement of their constitution. I am inclined to believe that psychotherapeutic measures and a greater attention to the mental health of the expectant mothers would be of substantial benefit to them, particularly to those with histories of "nervousness" during pregnancy, miscarriages and the birth of a mongol child. Patients with gross thyroid dysfunction, in addition to receiving the appropriate hormonal therapy as well as those afflicted with diabetes mellitus, should be advised to consult a psychiatrist. The psychotherapy received in the course of the pregnancy should materially influence the patient's mental condition and outcome of the pregnancy.

SUMMARY

This investigation draws the attention to the finding that there exists a higher incidence of endocrine disorders in mothers of mongol children than in mothers of normal offsprings. Six endocrine disorders comprising 3 cases of diabetes mellitus, 2 cases of Graves' disease and 1 of myxoedema, as well as 23 cases of miscarriage, were found in 42 mothers of mongol children—study group—as against 2 major endocrine disorders, one being Graves' disease, one of diabetes mellitus, and nine miscarriages in a similar number of mothers of normal children—control group.

The incidence of hormonal insufficiency in the study group amounted to 14·2 per cent. as compared to 4·7 per cent. in the control group, the ratio being almost 3 : 1.

This study, although only based on a limited number of cases, tends to support the view that mongolism arises in a mother who has inherited a constitutional endocrine disturbance, most probably of a diencephalic origin.

The inadequate psycho-endocrine stimulation from that part of the brain on a dysplastic ovum is most likely to create intra-uterine environment which, in addition to nutritional deprivations, favours this developmental disorder.

Prophylactic and psychotherapeutic measures are recommended in all expectant mothers showing menstrual irregularities, neurosis and major endocrine disorders, as well as those who have given birth to mongol children.

The higher incidence and risks of the birth of a mongol child during the menopause has likewise been stressed.

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A CONTROLLED TRIAL OF RESERPINE IN CHRONIC SCHIZOPHRENIA

By

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UNCONTROLLED TRIALS

SINCE the introduction of reserpine by Kline in 1954 there have been relatively few studies of its use in schizophrenia and most of these have been uncontrolled. It is characteristic of these uncontrolled trials that when the results are assessed, they are described in glowing terms, and the percentage of patients reported as showing "moderate" or "marked" improvement is high.

For early investigators the figures are:

					Marked or Moderate Improvement
Noce, Williams, and Rapaport (1955)	..	..	..	..	64%
Barsa and Kline (1955) (total)	..	..	..	..	62%
Hollister <i>et al.</i> (1955)	..	..	..	..	46%
Kinross-Wright (1955)	..	..	..	..	70%
Tasher and Chermak (1955)	..	..	..	..	64%

More recently Moore and Martin (1957) reports a similarly uncontrolled study. Out of 22 chronic deteriorated schizophrenics they find "improvement" in 12; while out of 21 acute schizophrenics they find "much improvement" in 18.

CONTROLLED TRIALS

When trials are controlled a quite different picture emerges. Outstanding among the early investigators, Campden-Main and Wegielsky (1955) found no difference between patients having reserpine and patients on placebo tablets. Finn *et al.* (1955) reached a similar conclusion. Shepherd and Watt (1956) found that reserpine gave results which were even worse than those given by the placebo.

The only optimistic report in a controlled trial has been that of Naidoo (1956). He investigated the effect of reserpine and E.C.T., in the same trial, either separately or combined, and with a placebo control.

He found that reserpine alone produced:

25 per cent. marked improvements;

50 per cent. moderate or mild improvements;

25 per cent. not improved but easier to nurse;

with no improvements in the placebo group.

He thought that E.C.T. given with the reserpine gave a more rapid improvement at first, but that the final results were little better than without it. E.C.T. alone in this group gave only a mild degree of improvement.

It was therefore proposed to repeat Naidoo's work, expressing the results as a week-by-week variable, but using a more carefully designed rating-scale.

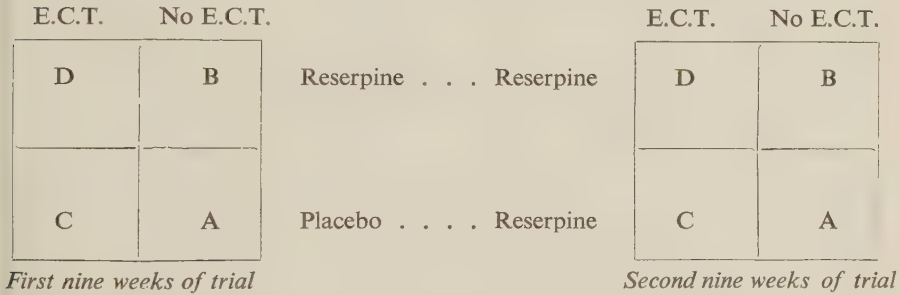
MATERIALS AND METHODS

All patients in the trial were females, from a chronic (but not refractory) ward. Those patients who were being treated currently, in any way, were not considered for the trial. Patients over seventy years of age were excluded. This gave thirty-two patients who were having no treatment at the time and in fact had had very little treatment in the past. They were divided into four groups matched as far as possible for age, length of illness and stay in hospital.

By random methods of allocation, two of these groups were put on reserpine and the other two on placebo tablets. One of the reserpine groups and one of the placebo groups was given E.C.T. from beginning to end of the trial.

The trial lasted eighteen weeks, and halfway through, i.e. at the beginning of Week 10, the patients then on placebo were changed to reserpine. Patients having reserpine were left unchanged.

In diagram:



Dosage of reserpine was: In the first two weeks 6 mg. orally and 2.5 mg. intramuscularly per day; thereafter 6 mg. or less orally per day and nothing intramuscularly. If side-effects were troublesome the oral dose was cut down as necessary and resumed later. *Dosage of E.C.T.* was twice a week at first and then less, depending on its effects. Patients who showed confusion and forgetfulness, or excessive euphoria, had their dose reduced.

Each group, A, B, C or D, originally had eight members, but three patients dropped out during the trial for reasons unrelated to it, making the groups uneven.

Group	No. in Group	Average Age in Years	Average Length Illness Years	Average Stay in Hospital Years
A	7	57	26	21
B	8	55	28	25
C	8	55	25	18
D	6	57	29	24
All groups	..	56	27	22

SYSTEM OF RATING

Each patient was seen once a week and rated for six aspects of her condition by myself and the nursing staff jointly. The first rating was done before the trial started. Also, when the trial was started a "note" was written (i.e. a statement

of the patient's clinical condition) and this was compared with a similar note written at the end of the trial.

The six aspects rated weekly were:

Coherence of thinking	}	The "Medical" aspect of the patient.
Communicativeness		
Affect		
General helpfulness	}	The "Nursing" aspect of the patient.
Suitability for different wards		
Suitability for various degrees of parole and discharge		

In each category the lowest weekly score was 0 and the highest 4, giving a total maximum obtainable of 24. The scale for rating is appended below. It will be seen that the lowest score, 0, represents a patient who is about as mad as can be, whereas the highest, 24, is barely distinguishable from complete sanity.

RATING SCALE

The numbers appended represent the value given to each rating, as a weekly mark.

RATING SCALE

The numbers appended represent the value given to each rating, as a weekly mark.

Coherence	Communicativeness	Affect	Helpfulness	Warding	Discharge-ability
0. Entirely incoherent. Blocks freely. Very deluded.	0. Entirely uncommunicative.	0. Absent or entirely incongruous.	0. Needs all nursing care and attention.	0. Suitable for refractory ward.	0. Not reliable outside hospital.
1. Much incoherence, blocking and delusions.	1. Usually withdrawn but communicative occasionally.	1. Much reduced or mostly incongruous.	1. Needs some supervision.	1. Suitable for ordinary ward.	1. Fit for occasional leaves.
2. Moderately incoherent, etc.	2. As often communicative as withdrawn.	2. Moderately reduced or moderately incongruous.	2. No special trouble. Can look after self.	2. Suitable for quiet closed ward.	2. Fit to go often on leave.
3. Slightly incoherent, etc.	3. Usually communicative, but occasionally withdrawn.	3. Slightly reduced or slightly incongruous.	3. Looks after self and is partly helpful to others.	3. Suitable for open ward.	3. Suitable for trial out of hospital.
4. Entirely coherent. No blocking. Not deluded.	4. Always communicates freely.	4. Normal.	4. Entirely helpful socially.	4. Can be left to self entirely. Entirely reliable.	4. Suitable for outright discharge.

It will be seen that each patient in the trial therefore got a weekly mark representing their clinical condition on a theoretically absolute scale. This made it all the easier to assess progress on the conventional scale of "slight", "moderate" and "much" improvement.

The table which follows shows this.

Groups not having E.C.T.

Group A		First nine weeks	Second nine weeks
Patient No.		Placebo	Reserpine
1		No change	No change
2		" "	" "
3		" "	Slightly improved
4		" "	No change
5		" "	" "
6		" "	" "
7		" "	" "

<i>Group B</i>	<i>Reserpine</i>	<i>Reserpine</i>
Patient No. 1	No change	No change
2	" "	" "
3	" "	"Slightly" improved
4	Slightly improved	" "
5	" "	Moderately improved
6	" "	Slightly improved
7	No change	No change
8	Slightly improved	Slightly improved

Groups having E.C.T.

<i>Group C</i>	First nine weeks <i>Placebo</i>	Second nine weeks <i>Reserpine</i>
Patient No. 1	No change	Much improved
2	" "	No change
3	" "	Slightly improved
4	" "	No change
5	" "	" "
6	" "	" "
7	" "	" "
8	" "	Much improved

<i>Group D</i>	<i>Reserpine</i>	<i>Reserpine</i>
Patient No. 1	No change	No change
2	Much improved	Much improved
3	No change	No change
4	" "	Moderately improved
5	" "	No change
6	" "	" "

RESULTS

1. In general the improvement in all patients is slight. At the end of the trial, out of 29 patients all having had at least nine weeks' reserpine, of whom 14 had E.C.T. in addition, the figures are:

No change	Slight Improvement	Moderate Improvement	Much Improvement	Total
18	6	2	3	29

2. If we take the figures for E.C.T. groups and non-E.C.T. groups separately we have:

	No Change	Slight Improvement	Moderate Improvement	Much Improvement	Total
Groups A & B (no E.C.T.)	9	5	1	—	15
Groups C & D (E.C.T.)	9	1	1	3	14

This difference is not significant at the 0.1 level.
($\chi^2 = 5.7$)

3. If we take the figures for reserpine and placebo groups, during the first nine weeks, for which they are comparable, we have:

	No Change	Slight Improvement	Moderate Improvement	Much Improvement	Total
Groups A & C (placebo)	15	—	—	—	15
Groups B & D (reserpine)	9	4	—	1	14

This difference is again not significant at the 0.1 level.
($\chi^2 = 6.07$)

CONCLUSIONS

1. The effect of reserpine, as measured during the first nine weeks of the trial, is not significantly better than that of placebo.
2. Groups which are given E.C.T. in addition to reserpine are not significantly better than those without E.C.T.

SUMMARY

Thirty-nine female chronic schizophrenic patients were treated variously with placebo, E.C.T. and reserpine.

The results provide no evidence that reserpine has any great place in the treatment of chronic schizophrenia.

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A COMPARISON BETWEEN PROCHLORPERAZINE AND CHLORPROMAZINE IN MENTAL DEFICIENCY

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INTRODUCTION

TRANQUILLIZING drugs that have been used in mental deficiency include reserpine, chlorpromazine, promazine, mepazine, hydroxyzine and prochlorperazine.

Esen and Durling (1) thought that the tranquillizing drugs in general were a useful preliminary to psychotherapy. However, the response to individual drugs has been variable.

Using *reserpine*, Johnston and Martin (2) found 49 out of 60 defectives showed some improvement. Horenstein (3) found the same with 9 out of 12 and thought the lower grades showed a better response. G. R. Sprogis *et al.* (4) agreed, finding improvement in 67 out of 70.

Using *chlorpromazine* the comparative figures for improvement were Johnston and Martin, 23 out of 27; Horenstein, 9 out of 12; Sprogis, 57 out of 59.

According to G. Tarjan *et al.* (5), 70–80 per cent. of 278 defectives showed some improvement with chlorpromazine; Adamson *et al.* (6) found 32 out of 40, and the present author, Robb (7), 36 out of 42 improved.

Blair and Harold (8) stated that only 1 out of 10 hyperactive mentally retarded children did not improve.

With *mepazine* Gillie (9) reported little change in 30 low-grade patients.

With *promazine* Bergin and Bergin (10) thought that epileptic defectiveness showed the most marked improvement.

Using *hydroxyzine* Craft (11) found no change in 23 low-grade patients.

With *prochlorperazine* Pilkington (12) reported appreciable improvement in 65 per cent. of 88 defectives. The response was most marked amongst those exhibiting simple hyperactivity and affective disorders.

Kline *et al.* (13) found that 2 defectives with psychosis showed no response and that one other was slightly improved.

According to F. A. Freyhan (14) 6 improved and one did not. A. Achaintre *et al.* (15) reported improvement in 6 out of 13 defective schizophrenics.

The purpose of the present trial was to assess the merits of prochlorperazine relative to chlorpromazine by exhibiting it to 23 mental defectives whose response to chlorpromazine was known.

PROCEDURE AND DOSAGE

Selection of Patients

There were 17 female patients (7 high grade and 10 low grade) and 6 male patients (2 high grade and 4 low grade).

The low grades were hyperactive, restless and destructive. The high grades were irritable, quarrelsome, impulsive and emotionally labile.

Their ages ranged from 17 to 48 years—the average age being 28 years. They included four epileptics; one low-grade male; and one high-grade and two low-grade females.

Dosage

The dosage of prochlorperazine was 100 mg. daily, given as 4×25 mg. tablets ("Stemetil"). This dosage was maintained for 11 weeks, being reduced only to counter side-effects.

ASSESSMENT OF RESULTS

The results were assessed from daily and weekly reports of the senior nursing staff and from weekly clinical assessments.

Four categories were used:

"Marked Improvement" if they could no longer be distinguished from more stable companions by behaviour alone.

"Slightly Improved" if their outbursts became more sporadic.

"No Change".

"Worse".

Special attention was paid to the presence or absence of aggressive hyperactivity; destructiveness and impulsiveness; and also to the presence of drowsiness; tremor; salivation; and of other signs of Parkinsonian picture.

RESULTS

(1) On prochlorperazine 100 mg. daily:

			Much Improved	Slightly Improved	No Change	Worse
Male:						
High Grade	..	..	—	1	1	—
Low Grade	..	..	—	—	4	—
Female:						
High Grade	..	..	1	6	—	—
Low Grade	..	..	—	4	4	2
Total	..	..	1	11	9	2=23

(2) Comparative figures for the same patients on 300 mg. chlorpromazine by mouth daily, were:

			Much Improved	Slightly Improved	No Change	Worse
Male:						
High Grade	..	..	—	1	1	—
Low Grade	..	..	—	1	3	—
Female:						
High Grade	..	..	—	7	—	—
Low Grade	..	..	—	4	6	—
Total	..	..	—	13	10	—=23

Two low-grade patients who had shown slight improvement with chlorpromazine were worse with prochlorperazine; as also was a low-grade patient who had been unchanged on chlorpromazine.

One high-grade patient who was slightly improved on chlorpromazine was much improved on prochlorperazine.

The overall picture, irrespective of grade was as follows:

		Some Improvement	No Change	Worse
Prochlorperazine	..	12 (52.2%)	9 (39.1%)	2 (8.7%)
Chlorpromazine	..	13 (56.5%)	10 (43.5%)	

For both drugs, the figures for improvement are lower here than in the series quoted earlier. In those, the figures for improvement were: for prochlorperazine 63 per cent. (70 out of 111), and for chlorpromazine 77 per cent. (360 out of 468).

SIDE-EFFECTS

There was no agranulocytosis, jaundice, skin rashes, photosensitivity or excessive weight gain.

There was no increase in the incidence of seizures amongst the epileptics in the series—but they were kept on their anticonvulsant medication throughout. However, one female with no previous history of epilepsy had an epileptiform seizure during treatment.

Five females became dull, drowsy, lethargic with salivation, tremor, and "Parkinsonian" picture. Two other females showed tremor only and another only salivation.

These side-effects were treated by dose reduction and by giving 50 mg. promezathine parenterally. Recurrence seemed to be prevented by oral administration of 25–50 mg. promezathine daily. These side-effects did not seem to be related to the therapeutic response.

CONCLUSIONS

Because of the small numbers involved, only general conclusions can be drawn, namely:

- (1) Prochlorperazine, in the dosage used, may be of help in some mental defectives who have not responded to chlorpromazine and may sometimes enhance improvement already exhibited.
- (2) Apart from the patients already mentioned it did not seem to lead to the drowsiness of chlorpromazine.
- (3) The side-effects may alarm patient's relatives and it is not recommended in this dosage for use outside hospital without supervision.

SUMMARY

Prochlorperazine in a dosage of 100 mg. daily was given to 23 mental defectives for 11 weeks. 52.2 per cent. showed some improvement. The comparable figure for chlorpromazine was 56.5 per cent.

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PHENOTHIAZINE SIDE-EFFECTS

COMPARISON OF TWO MAJOR TRANQUILLIZERS

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IN the six years since Delay and his associates first used chlorpromazine in psychiatry, at least forty-eight separate side-effects have been attributed to the drug. While many of these are minor, and indeed the majority are readily controlled in in-patients, the search for a phenothiazine of therapeutic value equal to or better than chlorpromazine, but with less or no side-effects, is well worth while. In out-patients there are two reasons for taking side-effects seriously. Firstly, they frequently lead to the patient ceasing to take the drug and thus relapse may occur. Secondly, they may be dangerous or even fatal if unreported—for example the signs of agranulocytosis.

We chose to compare chlorpromazine with a relatively new phenothiazine derivative, thioridazine (Melleril or Mellaril, Sandoz). Thioridazine is 3-methyl-mercapto-10-{2'-[N-methyl-piperidyl-(2'')]-ethyl-(1')}-phenothiazine, usually provided as the hydrochloride. Chlorpromazine is well established as a therapeutic agent and therefore serves as a good standard for comparison.

The structural formulae of chlorpromazine and thioridazine are shown in Fig. 1 overleaf.

There are three main groups of phenothiazines and they may be described according to the side-chains in each (Hippius and Kanig, 1958).

The first is the dimethyl group, with a propyl side-chain. Chlorpromazine is the most widely used member of this group. The second is the piperazine group, having a piperazinyl propyl side-chain. Typical members are perphenazine ("Trilafon"), prochlorperazine ("Stemetil"), and trifluoperazine ("Stelazine"). The third group has either a piperidyl-methyl or piperidyl-ethyl side-chain. Such a drug is thioridazine.

The piperazine group includes very potent drugs—these have less adrenergic and anticholinergic activity than the drugs in the dimethyl group, but they produce many and often marked extrapyramidal effects. By substituting a piperidine ring for a piperazine ring there was no increase in potency but the compound appeared to lose both its anti-emetic and its extrapyramidal effects (Kinross-Wright, 1959). One such drug (NP-207) was toxic to the retina. Replacing the halogen atom at the 2-position by a sulphur-containing radical

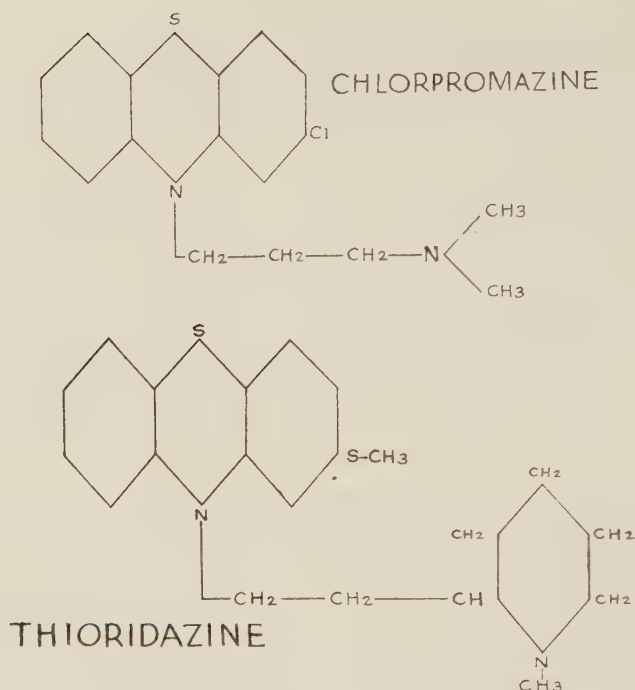


FIG. 1.

appears to have overcome the toxicity to the retina but retained all the other desirable properties—this is thioridazine.

The paucity of side-effects with thioridazine has been commented on by Cohen (1958), Fleeson *et al.* (1958), Remy (1958), Azima *et al.* (1959), Brunold (1959), Delay *et al.* (1959), Furtado (1959), Haug (1959), Judah *et al.* (1959), Kinross-Wright (1959) and Mayer (1959). Only Sauter (1959) states the contrary: “the side-effects were similar to those of other phenothiazines”. Therefore we decided to investigate the nature and severity of side-effects with equivalent therapeutic doses of chlorpromazine and thioridazine in a group of in-patients.

METHOD

Sample

This was restricted to patients in long-stay wards who had received or were receiving a phenothiazine to control their periodically disturbed behaviour and to facilitate their nursing. Sixty patients were selected from similar wards (22 being moved to the treatment ward in the three weeks before the trial began) who were all females in the 20–60 age group, and reasonably homogeneous as far as diagnosis and prognosis were concerned. Fifty-six were suffering from schizophrenic or “paraphrenic” psychoses and 4 were manic-depressives.

As it was known that some months would be needed to evaluate the two drugs, patients were selected who were extremely unlikely to leave hospital during that time. Clinically, many showed much evidence of deterioration, many were grossly delusional, often with hallucinations, and their prognoses were considered very poor.

PROCEDURE

The sixty patients were taken off all drug treatment for one month. They were then assessed by one of us (D.M.S.) and the ward sister on the L-M Fergus Falls Behaviour Rating Scale (Lucero and Meyer, 1951), a rating scale described by these authors as suitable for use in mental hospitals. The L-M Fergus Falls Behaviour Rating Scale measures eleven aspects of behaviour, each of which is described by a five-point scale. The scale is so designed as to be usable by relatively untrained raters. Areas of behaviour measured by the scale include attitude to work and occupational therapy, response to meals, response to other persons (e.g. fellow patients, nurses and doctors), attention to dress, psychomotor activity, speech and toilet behaviour.

Four groups of fifteen were then matched by the psychologist (G.D.G.) according to the following criteria: total score on the above rating scale, age and duration of illness. In addition an attempt was made to include in each group an approximately equal number of patients attending occupational therapy and of patients who were described as "incontinent", "deteriorated" and "inaccessible".

A doctor who had no duties connected with the ward concerned allotted each of the groups to a particular therapy—by random choice: chlorpromazine, chlorpromazine placebo, thioridazine and thioridazine placebo. The two placebos were identical in appearance with the respective active tablets. The mean score of patients on the rating scale, the mean age and the mean duration of illness are given below (Table I):

TABLE I
Comparative Rating of Groups Before Trial

		Chlor- promazine	Thiori- dazine	Chlor- promazine Placebo	Thiori- dazine Placebo	Total Sample
Mean total score Fergus Falls	..	21.60	21.73	22.03	21.80	21.79
Mean age		41.0 years	41.3 years	41.4 years	40.3 years	41.0 years (range 24-58)
Mean duration of illness		10 years	10 years	9.5 years	8.45 years	9.5 years (range 3½ months-29 years)

The rating for response to electro-convulsive or insulin therapy has been omitted—these treatments were of course not used during the period. The occupational therapy rating has also been omitted because objective assessment by the raters was not practicable.

The dosage was as follows:

First 4 days: 200 mg. per day
 Next 4 days: 300 mg. per day
 Next 21 days: 400 mg. per day
 Next 4 days: 600 mg. per day
 Next 5 days: 700 mg. per day
 Last 5 days: 800 mg. per day

43 days in all, total possible dose 20.3 grammes.

During the trial all patients were re-assessed on the rating scale by the same persons after two weeks and after six weeks, that is at the end of the trial.

There was daily observation and recording of side-effects and changes in behaviour by the psychiatrist, ward medical officer (P.H.C.) and nursing staff. Blood pressures and weights of patients were recorded before and during the trial and temperature and pulse charts drawn up.

It was planned that reduction of dosage when required by reason of severe side-effects would be by means of 100 mg. steps.

Special measures were taken to see that patients did not have any other drug treatment during the period, in particular for minor physical illnesses. Further, all tablets were swallowed in the presence of experienced nursing staff. Although a time-consuming procedure, it was felt that this was essential, as it has been reported that urine testing showed that as many as 10 per cent. of patients avoided taking their tablets (Pollack, 1958).

Nursing staff were given a list of all reported side-effects of both drugs and these were not differentiated. Nurses were drawn from a pool—all of them were informed that the side-effects of a new drug were being investigated and compared to those of chlorpromazine. They were not informed that placebos were being used. Even with "tranquillizing talks", nursing staff showed tremendous interest and enthusiasm, and one could readily forecast that some placebo improvement would occur.

At the end of the 43-day period, of the 15 patients in each group, 12 on chlorpromazine and 15 on thioridazine were further treated and observed for at least six weeks, and 12 chlorpromazine patients and 11 thioridazine patients for another 8 weeks.

RESULTS*

1. SIDE-EFFECTS

We compared the side-effects from two points of view, general differences and specific differences.

(i) General

Chlorpromazine produced many more side-effects than thioridazine, at all dosage levels and at all stages of the trial.

Four patients on chlorpromazine were necessarily limited in their dosage by reason of side-effects, one was progressively reduced from 400 mg. a day to 100 mg. and one from 600 mg. to 400 mg. Two patients were unable to tolerate above 600 mg. a day. Only one patient on thioridazine was reduced in dosage—from 700 to 600 mg. We were very fortunate that this patient, who had never

TABLE II
Comparison of Side-Effects

Side-Effect	Number of Patients	
	Chlorpromazine	Thioridazine
Photosensitivity reactions (severe)	10	Nil
Oedema of the face, especially eyelids	4	Nil
Parkinsonism (severe)	1	Nil
Depression (severe)	1	Nil
Somnolence (severe)	5	3
Dryness of mouth (severe)	1	1
Pallor and syncope	Nil	2
Tachycardia (above 120)	10	2
Pyrexia	4	1

before tolerated a phenothiazine, happened to be in the thioridazine group. She had had chlorpromazine (Largactil), promazine (Sparine), mepazine (Pacatal) and triflupromazine (Vesprin, Vespral).

(ii) *Specific*

The differences are summarized in Table II.

The word "severe" as used in the table indicates that such a patient would have taken herself off the medication if she were being treated on an out-patient basis.

Tachycardia and Pyrexia. Of the ten patients showing tachycardia above 120 on chlorpromazine, nine had other side-effects. The two thioridazine patients with tachycardia had pyrexia as well.

Increase in Weight. Significant weight gains occurred in both the active drug groups, after 4 weeks and after 6 weeks. The mean differences were:

Chlorpromazine: 4.8 and 6.0 pounds respectively.

Thioridazine: 3.2 and 4.6 pounds respectively.

In the control groups the mean differences were not statistically significant.

Blood Pressure. These readings were so irregular and inconsistent that it was not possible to draw any conclusions from them.

Photosensitivity. Each hot sunny day brought out a large number of reactions in chlorpromazine patients—all on 400 mg. a day or more—but none in thioridazine patients. In several patients the reaction was extremely severe and took many days to clear up.

Somnolence. With thioridazine this occurred in two patients on 200 mg. a day, and in one at 700 mg. (this was the patient whose dose had to be reduced to 600 mg. a day). With chlorpromazine somnolence occurred at all dosage levels in five patients.

Syncope. Two syncopal attacks occurred with thioridazine—in one patient before the first dose of tablets in the morning, but she had been clumsy and had dropped things the day before (dose 400 mg. a day). The other patient had her syncopal attack one hour after a dose of 100 mg. Neither patient had subsequent attacks.

Parkinsonism. The one severe reaction occurred on the 13th day at 400 mg. a day of chlorpromazine. This was an unexpectedly low incidence of Parkinsonism.

Placebo "Side-Effects"

No patient on placebo was reduced in dosage because of side-effects. Nevertheless eight patients on thioridazine placebo and six on chlorpromazine placebo showed tachycardia (above 120) and instability of temperature regulation—up to 100.6° F. axillary. One patient on thioridazine placebo had an axillary temperature above 99.0° F. on 15 days of the 43-day trial.

2. THERAPEUTIC

These are summarized in Table III overleaf.

Chlorpromazine Group. The mean difference in score after two weeks was +2.10 and, after six weeks, +4.87. The difference is significant in each case—in the former at the .05 level of confidence and, in the latter, at the .001 level of confidence.

TABLE III
Response to Treatment

Mean Total Score Fergus Falls	Chlor- promazine	Thiori- dazine	Chlor- promazine Placebo	Thiori- dazine Placebo
Initial rating	21·60	21·73	22·03	21·80
2nd rating (after 2 weeks) ..	23·70	23·26	21·77	21·73
3rd rating (after 6 weeks) ..	26·47	24·06	21·20	23·93
4th rating (after further 6 weeks)	—	26·73	—	—

Thioridazine Group. The mean difference in score after 2 weeks was $+1·53$, after 6 weeks $+2·33$ and, at the end of the treatment period, $+5·0$. After 2 and 6 weeks, the difference is significant at the $·05$ level of confidence, and at the end of the treatment period, at the $·001$ level of confidence.

Chlorpromazine Placebo. The mean difference in score after 2 weeks was $-0·26$ and, after 6 weeks, $-0·83$. These differences are not statistically significant.

Thioridazine Placebo. The mean difference in score after 2 weeks was $-·07$ and, after 6 weeks, $+2·13$. These differences are not statistically significant.

Individual Results

It would appear from Table IV that chlorpromazine was slightly more

TABLE IV
Individual Results of Trial After 6 Weeks—Fergus Falls

Changes in Ratings on Fergus Falls During Trial	Chlor- promazine	Thiori- dazine	Number of Patients Chlor- promazine Placebo	Thiori- dazine Placebo
Much worse ($-8 \rightarrow$) ..	—	—	—	—
Worse ($-4 \rightarrow -7$)	—	—	4	3
Same ($-3 \rightarrow +3$)	5	9	7	8
Improved ($+4 \rightarrow +7$) ..	6	5	4	1
Much improved ($+8 \rightarrow$) ..	4	1	—	3

effective than thioridazine and that both chlorpromazine and thioridazine were more effective than their respective placebos. The differences, however, were too small to reach statistical significance. When, however, the response to the two active substances was combined and compared with the response to the two inert substances, the difference was significant at the $·05$ level of confidence.

Ratings Based on Day-by-Day Observations of the Patients (at 6 Weeks)

Patients were rated as 5 (much improved), 4 (improved), 3 (remains the same), 2 (worse) and 1 (much worse) on the basis of the clinical data which was gathered on a day-to-day basis during the period of the study by the psychiatrist concerned.

The ratings were as shown in Table V.

It would appear from the table that response to treatment was most favourable among those who received chlorpromazine and least favourable among those who received its placebo. The response to thioridazine would seem less impressive. The differences in each case, however, were too small to

TABLE V
Individual Results of Trial After 6 Weeks—Clinical Rating

Clinical Rating		Number of Patients			
		Chlorpromazine	Thioridazine	Chlorpromazine Placebo	Thioridazine Placebo
Much worse	(1)	.. —	—	1	—
Worse	(2)	.. 2	—	3	3
Same	(3)	.. 5	10	10	6
Improved	(4)	.. 6	5	1	6
Much improved	(5)	.. 2	—	—	—

reach statistical significance. Even when the ratings for the two active substances were combined and compared with the ratings for the two inert substances, the difference was not statistically significant.

FURTHER TREATMENT PERIOD

As described under procedure above, daily observations were continued on the majority of patients who had received either chlorpromazine or thioridazine, for periods up to 14 weeks from the end of the controlled trial.

Side-Effects

Chlorpromazine: 7 patients showed side-effects, including two cases of Parkinsonism. These latter were reduced in dosage from 600 and 800 mg. respectively.

Thioridazine: 1 patient only showed a side-effect (oedema of the face and eyelids but with no redness) despite maintenance of dosage at the 500–800 mg. per day level.

Therapeutic

The period after the controlled trial was primarily intended for the observation of side-effects. However, the opportunity was taken to assess clinically the improvement of the two active treatment groups—and as all thioridazine patients remained on the drug for at least six weeks they were rated again on the Fergus Falls Scale. As only eleven of the original fifteen patients remained on chlorpromazine they were not re-assessed on this scale.

The patients on both drugs maintained their condition. In addition three other patients on thioridazine improved. Dosage was from 500 to 800 mg. daily. As shown in Table III, the difference in scores on the Rating Scale (before the trial compared with 12 weeks later) is significant at the .001 level of confidence. Individual results on the scale showed that four patients remained the same, nine patients improved and two patients were much improved.

SUMMARY AND CONCLUSIONS

1. A controlled trial lasting six weeks was carried out on 60 female patients in the long stay wards of a mental hospital to compare the side-effects of chlorpromazine and thioridazine.

2. In this group of female patients, almost all chronic schizophrenics, and all with poor prognoses:

- (i) Thioridazine produced far less side-effects than chlorpromazine at all doses between 200 and 800 mg. a day, at all stages of the trial, and during a subsequent period up to 20 weeks in all.

- (ii) Thioridazine did not produce photosensitivity, Parkinsonism or depression.
- (iii) Thioridazine was slower to act and required higher dosage than chlorpromazine. Results achieved with chlorpromazine in 6 weeks took some 12 weeks with thioridazine. Dosages of 600–800 mg. per day of thioridazine were roughly equivalent to 400 mg. per day of chlorpromazine.
- (iv) The unexpected therapeutic response with thioridazine in these patients warrants its further trial in patients who are unable to tolerate chlorpromazine or who have failed to benefit from it.

3. Thioridazine is so well tolerated that it appears an excellent phenothiazine for ambulatory patients, in particular for maintenance of patients after they leave hospital.

4. Instability of temperature regulation was shown so frequently by patients on placebos that it seems unlikely to be a significant side-effect of the phenothiazines, that is when it occurs in isolation.

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ENDOGENOUS DEPRESSION TREATED WITH IPRONIAZID—A FOLLOW-UP STUDY

By

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A DOUBLE-BLIND controlled trial of iproniazid in endogenous depression and a comparison of its effects with those of E.C.T. was reported in this journal by Kiloh *et al.* (1960). To summarize the results—of 26 patients treated with iproniazid a good immediate response was found in 14 cases (54 per cent.) whereas only 3 of 28 patients (11 per cent.) given placebo tablets showed a significant improvement at the end of three weeks. Of 27 patients treated with E.C.T. 24 (89 per cent.) showed a good immediate response.

To date (April, 1960) only four trials have been traced in which an attempt has been made to control the study. Freymuth *et al.* (1959) carried out a double-blind trial with 64 chronic regressed schizophrenics. Of 32 cases receiving 150 mg. iproniazid daily for eight weeks, 20 per cent. improved in regard to apathy and depression and 50 per cent. showed an increase in alertness and spontaneity but became more tense and aggressive. Only 2 of the 32 controls showed "some behavioural improvement".

Hoshino and Cease (1958) carried out a similar trial on 64 chronic hospitalized schizophrenics who were described as "stabilized"; in other words they had had no active treatment during the previous six months. The dose of iproniazid given was 150 mg. daily. No difference was found between the active and control groups.

Cole *et al.* (1959) treated 89 patients belonging to several diagnostic categories all having depression as an important symptom. The cases were allocated to three groups, the choice of treatment being iproniazid, placebo and psychotherapy, the latter varying according to the therapist involved. The trial was remarkable for the large number of cases that defaulted during treatment, 39 in all, more or less equally distributed between the three groups. The authors found no difference in the efficacy of the three forms of treatment.

Pare and Sandler (1959) carried out a trial of iproniazid on 50 patients suffering from "depression, who had been considered suitable for E.C.T.". The dosage given ranged from 150 to 450 mg. daily and the duration of treatment varied from two to forty weeks. It was a trial of the cross-over variety and

apparently was not blind. It is not clear from the paper how many patients were given placebo and the statement is made that "placebo was substituted in certain cases". The periods for which active and placebo treatment were given are not indicated. Twenty-six of the 50 patients improved on iproniazid but because 14 of these did not relapse when placebo was substituted, they were regarded as showing "coincidental improvement". This would seem to be a very high proportion of spontaneous recoveries amongst a group of depressive patients whose condition was thought to warrant E.C.T. In addition it assumes that the initial period of iproniazid treatment—the length of which is not stated—cannot lead to permanent amelioration of the depressive illness or to improvement sustained for the duration of placebo administration.

The surprising fact is therefore that in spite of the extensive literature on the use of iproniazid in psychiatry, amounting now to over 1,000 papers, no further double-blind studies of the effects of iproniazid on depression have been published. This seems regrettable.

All cases included in our trial have been followed up for at least six months from the termination of their initial three-week period of treatment. The clinical state of each patient was re-assessed at three and again at six months.

CASES TREATED WITH IPRONIAZID

Of the 14 cases treated successfully with iproniazid, 10 remained well after three months and 9 after six months. Of the 5 cases that relapsed, 2 were still taking iproniazid at the time their symptoms returned, one after six weeks and the other after ten weeks. The other three cases relapsed after they ceased to take the tablets. One patient took iproniazid for four weeks and relapsed after a further two months; the second stopped after six weeks and relapsed three months later; and the third ceased to take tablets after four months and relapsed in two weeks.

A further 4 cases, three of whom were placebo failures and one an E.C.T. failure, were treated with iproniazid. One of these showed no response, the other 3 responded well and their improvement was maintained at six months. One of the latter cases had treatment for only one month, the others were still taking iproniazid at six months.

Duration of administration of iproniazid. Including those patients who were given iproniazid as a second line of treatment, 12 out of 30 cases remained well at six months. Of these, 8 were still taking iproniazid. The duration of administration of the drug in the other four cases ranged from one month to four months. It is still not clear how long it is necessary to continue the administration of iproniazid in order to avoid the danger of relapse. There is little help on this point to be obtained from the literature. Scanlon (1959) gave the drug for periods varying from two weeks to fifteen months. Joel (1959) found that in 48 of 57 cases of manic depressive psychosis, a favourable result was obtained with iproniazid; 38 cases were still taking iproniazid after periods varying from two to twenty months (in 16 cases for fifteen to twenty months) while ten cases had ceased to take the drug after periods of administration varying from two to ten months. In a further group of 49 cases of manic depressive illness, 45 showed a favourable response to iproniazid. In 28 of these the average duration of treatment was four months and they were well after follow-up periods ranging from 1–16 months (in 14 cases from 10–16 months). The remaining 17 cases were still taking iproniazid at the end of the study.

Alexander and Berkley (1959) state that of 24 successfully treated patients,

13 received iproniazid for an average of 22 weeks while the other 11 continued to take the drug after 45 weeks. Hawkins *et al.* (1959) suggested that the drug should be stopped 3-4 months after improvement had occurred.

It seems likely that the optimum period of administration of iproniazid is an individual matter and may vary from a few weeks to a year or more. One case—not included in this trial—a severe endogenous depression, made an excellent response to iproniazid and indeed became slightly hypomanic. Two attempts to stop the tablets at six and nine months were made and were promptly followed by a return of the depression. The symptoms disappeared when the iproniazid was re-instituted. Finally, after fourteen months on the drug, the patient's symptoms returned in full force although he was still taking 150 mg. of iproniazid daily. On this occasion he responded well to imipramine. The duration of treatment must be influenced by the natural periodicity of depressive illness. The suggestion has indeed been made that the only effect of anti-depressive drugs is to control symptoms until spontaneous recovery occurs. This view is difficult to refute without controlling the trial for a period of six months or longer—a procedure which would be difficult to justify on ethical grounds. Experience with the drug suggests that it achieves something more than mere symptomatic relief whilst the natural history of the illness evolves.

It seems that if iproniazid is given for a depressive illness, one should anticipate a period of administration of at least four to six months. After this time an attempt can be made to discontinue the drug but in many cases this will prove premature.

CASES TREATED WITH E.C.T.

The relapse rate amongst cases treated initially with E.C.T. was high. Within three months, 9 of the 24 improved cases had relapsed and by six months a further two cases showed a return of symptoms. At six months, therefore, the success rate of E.C.T. had fallen from 89 per cent. to 48 per cent. In addition, E.C.T. was given as a second line of treatment to 25 cases who had failed to respond either to iproniazid or to placebo tablets. The relapse rate among these was of a similar order. In all, 49 of 52 cases (94 per cent.) given E.C.T. showed a good immediate response. Of these, 27 (52 per cent.) had relapsed within six months.

COMPARISON OF THE EFFECTS OF IPRONIAZID AND E.C.T.

Taking all the cases treated with iproniazid, a good immediate response was obtained in 17 out of 30 patients (57 per cent.). After six months, 12 of these cases (40 per cent. of the total; 71 per cent. of those initially improved) remained well.

With ECT, 49 out of 52 cases (94 per cent.) showed a good immediate response. After 6 months, 25 of these cases (48 per cent. of the total; 51 per cent. of these initially improved) remained well.

About one half of the cases treated with E.C.T. therefore had relapsed within a period of six months. The relapse rate following successful treatment with iproniazid was considerably less than this and after the six-month period the proportions of the two groups of cases remaining well became comparable.

Eight cases which failed to respond to iproniazid showed a good response to E.C.T. but only three of these remained well after six months. One case that relapsed after treatment with E.C.T. did well on iproniazid.

These figures are very small but they do tend to confirm the fact that

E.C.T. has an immediate superiority over iproniazid, though with the passage of time it becomes less marked. They suggest, too, that there are likely to be patients who respond to the one form of treatment but not to the other.

Other monoamine oxidase inhibitors are likely to have at least the same order of efficiency as iproniazid and experience has shown that imipramine is rather more effective (Ball and Kiloh, 1959). In view of the high relapse rate following E.C.T. and the relatively low relapse rate of patients on these drugs which make the final results of the two forms of treatment equable, it seems justifiable in the majority of cases of depression to give a course of one or other of these substances before proceeding to E.C.T.

SUMMARY

1. Although many more cases of endogenous depression show a good immediate response to E.C.T. than to iproniazid (94 per cent. as compared with 57 per cent.), the relapse rate in the six months following E.C.T. is such that after this time the response rate is comparable (48 per cent. as compared with 40 per cent.).

2. The optimal duration of treatment with iproniazid has not been satisfactorily established. In the majority of cases a period of administration of 4-6 months is likely to be necessary and in some the drug may have to be given for a year or longer.

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LEVOMEPRMAZINE IN THE TREATMENT OF NEUROLEPTIC RESISTANT PSYCHOTICS

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LEVOMEPRMAZINE, levo-3-methoxy-10(2' methyl-3'-dimethylamino-1' propyl) phenothiazine is a phenothiazine derivative which was isolated in the Rhone-Poulenc Laboratories and studied pharmacologically by Sigwald *et al.* (2) in 1956.

Early reports, Deschamps (1), on the use of this compound in psychiatric conditions indicate that it is of particular value in the treatment of patients refractory to other neuroleptic agents.

A limited trial was undertaken to assess its usefulness in such patients within the mental hospital setting.

SELECTION OF PATIENTS

One hundred chronically disturbed patients were selected for treatment. Eighty-six of the patients selected fell within the category of Schizophrenia, seven within the grouping Endogenous Depression, three were diagnosed Chronic Brain Syndrome, two Mental Deficiency and two Epilepsy with Psychosis. All patients had previously received other forms of therapy including seismotherapy, insulin shock therapy and other neuroleptic agents without appreciable benefit. The average age was thirty-nine years, minimum nineteen years, and maximum sixty-seven years. The duration of hospital stay ranged from two to thirty-one years with an average of seven years.

TREATMENT

Levomepromazine was administered by mouth in the form of 25 mg. tablets. Each patient commenced with an initial dose of 25 mg. twice daily, this dose being increased on alternate days by 25 mg. to a maximum of 600 mg. daily. The subsequent dosage necessary for the maintenance of optimal improvement was found in most patients to be of the order of 50 to 100 mg. daily.

The patient's ward environment remained constant throughout the duration of the trial. No measures other than drug administration were used during the period of the investigation.

RESULTS

For purposes of assessment, patients were rated according to the following criteria:

1. *Social Recovery.* Complete absence of psychotic symptoms. Rapid social and economic readjustment allowing of early discharge home.

2. *Much Improved*. Psychotic symptoms encapsulated and no longer apparent to the untrained observer. Socially more integrated allowing of the institution of rehabilitative measures and subsequent consideration of discharge from hospital on probation, and permitting the extension of such privileges as "leaves of absence" and "open ward" residence.
3. *Improved*. Partial remission of symptoms allowing the extension of parole privileges and facilitating ward management.
4. *Unimproved*. Self explanatory.
5. *Worse*. Regression to a level of adjustment inferior to that existing prior to the institution of therapy.

In only one case did improvement merit the application of the rating "Social Recovery".

Fifty-six patients manifested a lesser degree of improvement such that nineteen fell within the category "Much Improved" and thirty-eight within the category "Improved". Of the improved patients eleven were subsequently discharged from hospital.

Forty-one patients did not benefit from the therapy and were designated as unimproved.

Two patients, one epileptic and one defective, showed a marked deterioration following the commencement of medication. The former showed an increased impulsiveness and combativeness, whilst in the defective the deterioration was characterized by a reduction in spontaneity and the onset of excreta carelessness which had not previously been observed.

Discontinuation of Levomepromazine resulted in a rapid return to the pre-treatment level of adjustment.

With regard to diagnostic categories, no definite trends were observed which would indicate any distinct specificity of action of Levomepromazine.

Side-effects. Varying degrees of drowsiness were encountered in thirty-six of the patients. This was transient in all but one patient in whom psychomotor inhibition became so marked as to necessitate termination of therapy.

With doses in excess of 400 mg. daily, urinary retention was occasionally seen, necessitating reduction of dosage. Five patients complained of dizziness, two of dysphagia and one of oedema of the face. Four patients exhibited tremor which was confined to the hands, these benefited from the concomitant administration of benztropine methanesulphonate (Cogentin) in doses of the order of 1 mg. twice daily.

Weekly urinalysis failed to show any abnormalities throughout the duration of the study. Liver function tests remained within the normal limits and no blood dyscrasias were observed.

CONCLUSION

In this study, Levomepromazine was used to treat one hundred chronic psychotic patients who had not previously responded to other somatic therapies. Like its parent drug, chlorpromazine, Levomepromazine appears possessed of potent neuroleptic activity. Present indications are that Levomepromazine has a definite place in the treatment of a significant number of patients resistive to other therapies.

Side-effects are encountered fairly frequently but are seldom troublesome, requiring little more than a reduction of dosage; and only rarely interfering with therapy.

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A CONTROLLED TRIAL OF PHENELZINE IN DEPRESSIVE REACTIONS

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BETA-PHENYL ethyl hydrazine dihydrogen sulphate (phenelzine, "Nardil") is one of the group of hydrazides being currently advocated for the treatment of depression. It has been claimed that this drug has similar properties to iproniazid but is less toxic (Furst, 1959; Thal, 1959), and uncontrolled clinical trials have produced reports of rapid improvement in 70-80 per cent. of cases (Furst, 1959).

Reports of toxic symptoms and signs have now accumulated with wider usage. Kothari (1960) reports that seven out of thirteen patients on the drug developed disturbed liver function tests; King (1959) reports one death from a myocardial infarct after four weeks on the drug, one death from broncho-pneumonia and haemorrhagica gastrica after 45 days on the drug. One patient in this series developed thrombocytopenic purpura which cleared when the drug was stopped. Minor side-effects noted are orthostatic hypotension, ankle oedema, constipation and drug rash (Sainz, 1959; Kothari, 1960).

Opinions about combining this drug with electro-convulsive therapy (E.C.T.) differ. Sainz (1959) recommends at least four days free of the drug before E.C.T. is given, as the accumulation of catecholamines in the brain may lead to a cardiovascular accident. Bleaden and Czekanska (1960) report two cases of cardiovascular collapse in four patients treated with E.C.T. and phenelzine, but Frost *et al.* (1960) and Gilmour (1960) used this combination in a considerable number of cases without untoward effects.

Trials which employ some sort of controls appear less impressive as far as therapeutic results are concerned. King (1959) comparing E.C.T. and phenelzine concludes that "the study raises the question whether phenelzine is of any benefit in depression". Keith (1959) reports a clinical trial with several anti-depressants and appears to have found no advantage over placebo in the case of phenelzine.

The following study was designed to show any indications the drug might have in depressed in-patients.

METHOD

The trial was conducted in one of the three female admission units at Runwell Hospital and all admissions diagnosed as suffering from depressive reaction (regardless of subtype and of secondary features) were considered for treatment provided that two clinicians agreed on the major diagnosis after independent examination. When a case was in this way selected for the trial the management returned to the clinician in charge of the patient who then

decided whether this patient should be treated with E.C.T. or treated conservatively. The cases thus fell into two broad treatment groups and were hereafter dealt with in the trial in two different ways.

(a) Cases selected for conservative treatment were dealt with in a double-blind trial with each patient receiving two weeks' treatment with phenelzine in doses of 25 mg. t.d.s. for the first week, and 50 mg. t.d.s. for the second week in the absence of a satisfactory response. For a further two weeks these patients received matched placebo tablets (1-2 t.d.s.). The cases were treated in random order allocated by the pharmacist and neither the nursing staff nor the ward clinician who performed the ratings were aware of the active treatment period.

(b) Cases selected for E.C.T. were treated in one of three ways for two weeks. They were given either:

- (i) Bi-weekly E.C.T. (with Suxamethonium Bromide and hexobarbitone) and placebo tablets (1-2 tablets t.d.s.).
- (ii) Bi-weekly hexobarbitone injections to produce sleep and phenelzine tablets (25-50 mg. t.d.s.).
- (iii) Bi-weekly hexobarbitone injections to produce sleep and placebo tablets (1-2 tablets t.d.s.).

While the study was running as an open trial, treatment was allocated by the pharmacist by drawing cards from a shuffled pack with three suits which represented the treatments. As the negative results of the trial became apparent, however, the last two cases were allocated to the appropriate treatment group in order to obtain round numbers. In this trial the clinicians knew which patients received hexobarbitone injections and which E.C.T. They did not know however, which of the hexobarbitone treated patients received drug and which placebo. The patients on E.C.T. and those on hexobarbitone were treated in an identical manner at the same treatment sessions and were unaware of any differences in therapy. In this group the ratings were supplied by a research clinician who was examining the patients for other purposes and who was unaware of the treatments used.

Where night sedation was required all cases were given Sodium Amytal 3-6 gr.

Where agitation and subjective distress by day were severe and rapid symptomatic control was required Sodium Amytal 1-2 gr. t.d.s. was used. Eight patients were so treated and these are indicated later.

Thirty-one consecutive depressed admissions were considered. Clinical information is shown in Table I. It will be apparent that these patients were a severely affected group of psychotic depressives, and in view of the pressure on hospital beds the indications for admission necessarily implied that they were unsuitable for out-patient treatment (including out-patient E.C.T. as facilities for this were available).

One patient was not included in the trial because of Parkinsonism, thought to be of arteriosclerotic origin. Six other patients withdrew or were withdrawn from the trial—two in the conservative group and four in the active treatment group. In the conservative group two patients discharged themselves against advice—one while on drug, one while on placebo—both showing no improvement. In the active treatment group two patients on E.C.T. and one on hexobarbitone injections were withdrawn by the clinicians for physical complications

TABLE I

Symptomatology, Treatment and Actuarial Data of 31 Consecutive Depressive Female Admissions

		"Conservative" Trial	"Active" Trial	Patients Withdrawn	Total
Total Number in Group	..	12	12	7	31
Symptoms:					
Agitation		9	12	6	27
Retardation		5	7	3	15
Self reproach		7	4	4	15
Depressive delusions		5	3	3	11
Early morning waking		4	6	1	11
Other sleep disturbances		6	4	—	10
Hypochondriasis		2	3	4	9
Suicidal attempt before admission		1	—	3	4
Treatments:					
Received night sedation	..	10	7	4	21
Received day sedation	..	3	2	2	7
Actuarial Data:					
Mean age on admission	..	59.6	62.3	56	59.8
Mean age at first admission		46.5	59.6	47	48.4
Mean number of admissions		7	3	4.3	4.9

unrelated to the treatment used. A fourth patient on hexobarbitone injections discharged herself.

In the results which follow global assessments are used and the definitions of the terms employed are as follows:

1. *No change*—symptoms unchanged, or worse.
2. *Slight improvement*—affective disturbance showing no change and no change in primary symptoms, e.g. depressive delusions. Some improvement of secondary symptoms, e.g. anorexia.
3. *Moderate improvement*—some improvement of primary symptoms or great improvement of secondary symptoms.
4. *Great improvement*—marked improvement of primary and secondary symptoms.

These assessments are interpretations of fuller clinical examinations made by the clinician in charge of the patient or the research clinician.

RESULTS

A. CONSERVATIVE TREATMENT GROUP

Here each patient acted as her own control. Twelve patients in all were treated. The results are shown in Table II. Phenelzine appears to offer no advantage over placebo. Any improvement may in fact be related to length of stay in hospital and if the results in a fortnight are compared with those at the end of a month (Table III) a trend to this effect which does not reach accepted levels of significance is demonstrated.

TABLE II

Results of "Conservative" Treatment Trial in 12 Patients after 2-week Periods on Phenelzine or Placebo

		No Change	Slight Improvement	Moderate Improvement	Great Improvement	Totals
Drug	..	5**	5*	1	1	12
Placebo	..	8***	—	2	2	12
Totals	..	13	5	3	3	24

(* Each asterisk indicates one Patient receiving Amylobarbitone Sodium 2 gr. t.d.s.)

TABLE III

Comparison of Results in "Conservative" Treatment Trial in 1st and 2nd Periods Regardless of Treatments Employed

			No Change and Slight Improvement	Moderate and Great Improvement
1st Period	..	..	11	1
2nd Period	..	..	7	5

B. ACTIVE TREATMENT GROUP

Again twelve patients were treated and the results at the end of a fortnight are shown in Table IV. The only patient showing any degree of improvement who was not treated with E.C.T. was, in fact, also receiving Sodium Amytal and placebo by day. The improvement registered was related to the relief of retardation and the change may be related to the barbiturate but not the hydrazide. After a further fortnight when the eight hexobarbitone patients started E.C.T. while those already on it continued or completed their course there is a significant shift to improvement in the results (Table V). This rating was taken from the patient's notes, however, and is not "blind" as far as the treatment is concerned.

TABLE IV

*Results after 2 Weeks in "Active" Treatment Trial,
i.e. 4 Modified E.C.T.s with Placebo, 4 Hexobarbitone Injections with Placebo,
or 4 Hexobarbitone Injections with Phenelzine*

	No Change	Slight Improvement	Moderate Improvement	Great Improvement	Totals
Number of Patients treated with:					
E.C.T. and Placebo	—	2	—	2	4
Hexobarbitone and Placebo	3	1*	—	—	4
Hexobarbitone and Phenelzine	4*	—	—	—	4
Totals	7	3	—	2	12

(* Each asterisk indicates one Patient receiving Amylobarbitone Sodium 1-2 gr. t.d.s.)

SIDE-EFFECTS

No serious side-effects were observed with phenelzine in this trial and a small number of patients had E.C.T. immediately after phenelzine without ill effect.

TABLE V

Results after 4 weeks in "Active" Treatment Trial, all Patients Having Received Modified E.C.T. bi-weekly in second fortnight

	No Change	Slight Improvement	Moderate Improvement	Great Improvement	Totals
Patients previously treated with:					
E.C.T. and Placebo	—	—	1	3	4
Hexobarbitone and Placebo	—	—	2	2	4
Hexobarbitone and Phenelzine	—	—	2	2	4
Totals	—	—	5	7	12

DISCUSSION

Interest in the hydrazides arose from the observation that isoniazid and iproniazid, used in the treatment of tuberculosis, possessed euphoriant qualities. Isoniazid was reported on by Salzer and Curie (1953) who claimed favourable results in the treatment of anxiety states and depression in 68·3 per cent. of cases and also that E.C.T. was avoided or the numbers of treatments reduced. Iproniazid, which was abandoned for the tuberculous because of its toxicity (Goodman and Gilman, 1955) has nevertheless had a wider trial in psychiatric cases. While early reports were hopeful, particularly as far as depressive reactions are concerned (Dally, 1958; West and Dally, 1959; Kline, 1958; Ayd, 1957) recent controlled studies are again either more cautious in assessing the percentage of patients helped (Pare and Sandler, 1959) or negative (Cole *et al.*, 1959).

While isoniazid is not an amine oxidase inhibitor, iproniazid possesses this property, and this fact has assumed a highly speculative aetiological importance in the minds of its advocates. As therapists are often inclined to see a tangible hypothesis of a drug's mode of action as further evidence of its efficaciousness, it should be stressed that because a number of new drugs are monoamine oxidase inhibitors there is as yet no valid reason to expect therapeutic success with their use. The clinical properties of such drugs can only be measured in clinical trials, and in the trial reported there seems little evidence that two weeks' treatment with phenelzine in doses of 25-50 mg. t.d.s. is of any value in psychotic depressive reactions.

SUMMARY

Twenty-four of thirty-one consecutive depressed female admissions completed a trial with phenelzine.

Twelve patients were selected for conservative treatment and were observed in a double-blind trial with two-week periods on drug and placebo. No advantage was found for the drug. Any improvement observed may have been related to length of hospital stay.

Twelve patients selected for E.C.T. were treated with either modified E.C.T. and placebo, hexobarbitone injections and phenelzine or hexobarbitone injections and placebo for two weeks bi-weekly. Only patients treated with E.C.T. showed appreciable change. No major toxic effects were observed in drug-treated patients.

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THE EFFECTS OF SODIUM AMYLOBARBITONE AND DEXAMPHETAMINE SULPHATE ON THE PERIPHERAL VISUAL FIELD

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IN an earlier investigation (Holland, 1960) the peripheral visual field was examined under three treatment conditions, namely meprobamate (2-methyl-2-n-propyl-1, 3 propanediol dicarbamate), Doriden (glutethimide), and no drug. Results from 24 subjects, each tested three times, indicated that there were significant differences, attributable to the treatments, in both the inner and outer discrimination thresholds and also in the magnitude of the interval of uncertainty between thresholds. In the present experiment it has been thought worth while to examine the visual field for the effects of two other compounds, a stimulant dexamphetamine sulphate (Dexedrine), and a depressant sodium amylobarbitone (Amytal).

THE PRESENT INVESTIGATION

When plotting the extent and sensitivity of the visual field by delineating intensity isopters, the problem for the subject is one of brightness discrimination. The discrimination threshold for the inner threshold is the point at which a judgment of "different" between target and background brightnesses can be made, and the outer threshold is the point at which an existing difference can no longer be resolved (Sharples, 1946; Mann, 1946). The present investigation can therefore be viewed in two ways: (a) the extent of the visual field; and (b) brightness discrimination changes; due to the action of the drugs used.

The number of meridians examined in the present investigation has been reduced from the earlier study. The nasal visual field has been ignored because of "nose plotting" and the upper and lower temporal field disregarded because of individual differences in lid, brow and cheek positions. In all other respects the present procedure is comparable with previous work.

SUBJECTS

There were 6 subjects, each seen on three separate occasions. They were all female, aged between 19 and 24 years. Not less than one and not more than four hours elapsed between taking the drug and being tested.

THE DRUGS

There were three treatments comprising two drugs and a placebo. All the capsules were identical in appearance and contained either dexamphetamine sulphate 10 mg., sodium amylobarbitone 3 grains (approximately 200 mg.), and a placebo. The treatments were administered according to a double latin square design, randomizing the orders in which they could occur and thus equating for differential practice effects.

THE INSTRUMENT

The perimeter employed was a commercially available Goldman projection perimeter,* which was modified to allow accuracy of direction while keeping the eye under continuous scrutiny. As normally supplied, accuracy of direction along the meridians is impaired unless some sacrifice is made of the continuous observation of the eye, or *vice versa*. By a small modification which involves the construction of a plastic channel, pivoted at a point near the centre, a specific spot along any meridian can be repeated while observation of the eye is maintained. The modification is useful in increasing the reliability for research purposes, it may not be necessary for ordinary ophthalmic uses.

PROCEDURE

The subject was seated at the apparatus and gross adjustments made. The head was strapped to the combined chin and head rest and depth of penetration of the face adjusted. Owing to differential face reflection the bowl illumination was set before each examination by use of filter and photometer screen. From the time that all adjustments had been made, a period of 4 minutes was allowed for light adaptation to the bowl level before testing began.

The subject reported the appearance or disappearance of the target light ($\cdot 25 \text{ mm}^2$, relative intensity = $\cdot 310$) by depressing a morse key with her right hand, which in turn illuminated a small bulb in front of the experimenter.† Practice trials were given on the first day until the subject was thoroughly conversant with the procedure, after which the incoming trials were plotted first, in random order, followed by the outgoing trials. In all, ten meridians of the left temporal field were tested, i.e. every $7\cdot 5^\circ$ between 210° and 135° inclusive, with the exception of the 180° meridian which was omitted for mechanical reasons.

RESULTS

The results of testing are presented in Tables I–III. Table I presents the means of the inner and outer threshold scores for the ten meridians measured. An examination of the scores by analyses of variance showed that there are no significant differences between drugs in the *inner threshold*, i.e. means = Placebo 65·5, Dexedrine 65·3, Amytal 65·5, $F = \cdot 0644$, but that there are highly significant differences due to drugs in the *outer threshold* scores. The outline of the analysis of outer threshold scores is presented in Table II. Three significant variances emerged, namely, those for people, treatments and trials, the first being individual differences in field size, the second defining the drug effect, and the third outlining the differential sensitivity of the meridians explored. When the total drug variance was broken down for paired comparisons only Placebo/Amytal and Dexedrine/Amytal could be discriminated with the required degree of confidence.

An analysis of the *interval of uncertainty* scores is presented in Table III. This score is derived by subtracting the inner threshold from the outer, along each of the ten meridians. In this analysis only two significant F ratios appear, those for *people and treatments*, both achieving the 1 per cent. level of confidence. The trial means for the interval of uncertainty were Placebo = $7\cdot 283^\circ$,

* The author would like to acknowledge his debt to the Central Research Fund Committee, University of London, for financial assistance in the purchase of the apparatus.

† This method of reporting obviated the head movement which occurs when the head is strapped to the chin-rest and a verbal response is required.

TABLE I
Perimetry
Trial Means

<i>Inner Threshold</i>			
Subjects	Placebo	Dexedrine	Amytal
1	71.7	71.8	71.2
2	66.9	66.4	64.8
3	65.5	67.4	68.1
4	68.5	68.4	67.8
5	66.6	65.2	67.4
6	53.9	52.8	53.8
Means	65.5	65.3	65.5
<i>Outer Threshold</i>			
Subjects	Placebo	Dexedrine	Amytal
1	77.3	76.5	78.9
2	71.3	69.7	73.0
3	73.8	73.9	77.3
4	78.0	79.2	80.9
5	72.9	71.9	76.4
6	63.2	60.8	65.2
Means	72.8	72.0	75.3

TABLE II
Perimetry

Outline of analysis of variance of *outer threshold* scores

Source	D.f.	M.S.V.	F.	P.
Between people	5	999.98	80.98	1%
Between treatments	2	177.61	14.38	1%
Between trials	9	825.08	66.81	1%
Between orders	2	2.27	0.18	—
Residual	161	12.349		
Total	179			

t, Placebo-Dexedrine = 1.168; N.S.
t, Placebo-Amytal = 3.940; 1%
t, Dexedrine-Amytal = 5.108; 1%

TABLE III
Perimetry

Outline of analysis of variance of *interval of uncertainty* scores

Source	D.f.	M.S.V.	F.	P.
Between people	5	141.94	26.49	1%
Between treatments	2	160.34	29.92	1%
Between trials	9	3.63	0.68	N.S.
Between orders	2	8.34	1.56	N.S.
Residual	161	5.359		
Total	179			

t, Placebo-Dexedrine = 1.418; N.S.
t, Placebo-Amytal = 5.871; 1%
t, Dexedrine-Amytal = 7.289; 1%

Dexedrine = 6.683° , and Amytal = 9.767° , *t* tests between them again indicating that although Placebo/Amytal and Dexedrine/Amytal differences were highly significant there was no difference between Placebo/Dexedrine.

Finally, as a check on whether there is a consistent change in the *interval of uncertainty* with a change in the target intensity, which is also effected by drugs, inner and outer thresholds were determined along a single meridian (187.5°) at three relative intensities ($.030$, $.096$, $.310$). The means for the three intensities independent of drug were: intensity 1 = 16.388° ; intensity 2 = 9.555° ; intensity 3 = 7.555° . When the three means are averaged for the drug conditions they result as follows: Placebo 11.111° ; Dexedrine 9.388° ; and Amytal 13.000° .

An outline of the analysis of variance of the scores is presented in Table IV. The main significant variance is again attributable to the drug effect, this time, however, only a *t* test between Dexedrine/Amytal gives a difference which is significant.

TABLE IV

Perimetry

Outline of analysis of variance of *intensity isopter interval of uncertainty* scores

Source	D.f.	M.S.V.	F.	P.
Between people . . .	5	10.12	0.92	N.S.
Between treatments . .	2	58.72	5.32	1%
Between trials . . .	2	386.17	34.98	1%
Between orders . . .	2	10.72	0.97	N.S.
Residual	42	11.04		
Total	53			

t, Placebo-Dexedrine = 1.555; N.S.

t, Placebo-Amytal = 1.705; N.S.

t, Dexedrine-Amytal = 3.260; 1%

SUMMARY AND CONCLUSIONS

The results of the present investigation differ slightly from the findings of the earlier study. In the earlier investigation both the ataractic, meprobamate, and the hypnotic, glutethimide, reduced the extent of the inner threshold of the visual field compared with the control, no-drug, condition. In this present study neither of the drug treatments changed the inner threshold sufficiently to produce a reliable difference. The outer threshold changes, on the other hand, are consistent with earlier findings, namely, the depressant drug Amytal has extended the visual field compared to the Placebo treatment. Again, as in the earlier study, the difference between the inner and outer threshold (the *interval of uncertainty*) demonstrates a profound change, attributable to the drugs. Finally, when the increase in the interval between thresholds is examined in relation to increasing target intensity, drug effects also emerge which indicate that Amytal enlarges the interval whereas Dexedrine narrows it.

The finding of an interval of uncertainty drug effect implies one of two possible explanations: (a) a slowing of motor response in reacting to decreases in stimulus intensity; or (b) some change in the sensory scale of discrimination of brightness differences; both explanations being based upon the central action of the drugs. The first of these explanations was considered after the first study but rejected owing to its incompatibility with other test findings

which required rapid responses. However, other authors who have been concerned with visual field reductions, under conditions of anoxia (Ikui, 1947), do not reject the possibility of general response slowing. The second explanation would involve an investigation of the psychological changes which may follow drug ingestion. Both explanations are, of course, questioned due to the finding that the drug effects only appear to manifest themselves to a decreasing intensity, i.e. an outgoing stimulus.

Finally, the present method of measurement does not permit discrimination between explanations as, clearly, the two factors of discrimination and response are confounded. An alternative method is called for in which brightness discrimination is not influenced by speed of response. Such measurements are available in the constant methods and future experiments will be attempted by their use. If drug effects can be demonstrated as inducing changes in psychosensory continua, integration into general psychological theory seems possible.

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TRIAL OF IMIPRAMINE

By

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ALTHOUGH in the majority of cases E.C.T. is swiftly effective in the treatment of morbid depression there are some who regard it with repugnance, and have long hoped for drugs which would obviate its use. It was that hope which prompted this trial of imipramine ("Tofranil").

The subjects of the trial were forty women in-patients of Middlewood Hospital, thirty-four of whom had been admitted recently whilst the remaining six had been in hospital for a considerable period. Their ages varied between forty-two years and seventy-five years and nineteen of these were aged over sixty years.

Whilst all suffered from a depressive state the primary condition in four was a chronic schizophrenia, in another paraphrenia and in another a personality disorder, and in four others dementia. The six long-term patients were amongst this number. The remaining thirty patients suffered from involutional melancholia.

Physical disabilities were common. Nine suffered from hypertension—diastolic pressure above 110 mg. of mercury—four suffered from cardiac disease, two from marked arteriosclerosis and four from a moderately severe anaemia.

TECHNIQUE

Before treatment commenced each patient was assessed on a five-point scale by Sister C. Winterbottom, Sister N. L. Simpson, and by Dr. Vera Holdway, for various aspects of the depressed condition. A controlled technique was used—half the patients being given Tofranil and half a placebo. When treatment had proceeded for about two weeks another assessment was made. The information as to which patients were having Tofranil and which the placebo was then divulged by the Chief Pharmacist. From then on, all patients received Tofranil with the exception of those who recovered whilst taking the placebo.

DOSAGE

On the 1st day Tofranil 50 mg. t.d.s. was given, increasing on the 2nd day to 75 mg. t.d.s. and on the third day to 100 mg. t.d.s. This dose remained unchanged for the following 10 days after which it was reduced by 25 mg. daily until a maintenance dose of 50 mg. was reached. Those patients who made a satisfactory response continued with this dose for a few weeks after discharge from hospital.

RESULTS

The correlation between the assessments made by the Sisters and Dr. Holdway was found to be as high as .8 and this despite the fact that each

looked only at her own assessment and did not discuss the patients in relation to them.

The first and second assessments were compared statistically (chi-square test using Yate's correction where appropriate) for both groups. The results are tabulated below:

Aspects of Depression	χ^2 Tofranil	χ^2 Placebo
1. General impression on observer of depression ..	8.56†	2.76
2. Facial expression of depression ..	2.7	0.02
3. Retardation	0	0
4. Agitation and tension	1.8	0
5. Activity	5.44*	2.7
6. Sociability	2.8	0.46
7. Extent to which deluded	5.34*	0
8. Ability to be interested	6.72†	1.5
9. Emotional liveliness	1.88	1.44
10. Expressions of guilt	1.0	0
11. Hopelessness	4.0*	0
12. Hypochondriasis	0	0

* = significant at a 0.05 level.

† = significant at a 0.01 level.

It was hoped to demonstrate in those taking Tofranil a general trend towards recovery that was stronger than could be accounted for by the natural sequence of events. We think that it can be fairly claimed that the result does so demonstrate the action of Tofranil in relieving depression.

As treatment progressed beyond the first two weeks it became necessary in some cases to give E.C.T. When patients appeared to be quite well, both to themselves, their relatives and to the hospital staff, or when all treatment failed to produce any further improvement, the cases were divided into three categories in relation to their response to Tofranil. Response was "good" when the patient appeared to be recovered from depression without resort to E.C.T. It was "fair" when a few E.C.T.s were needed to obtain a satisfactory result. Response was "poor" when a relatively large number of E.C.T.s had to be given.

Two patients on the placebo alone recovered on commencing treatment. The remaining thirty-eight were divided as follows:

	Good	Fair	Poor
Patients on Tofranil from the onset	8	4	8
Patients initially on the placebo	5	5	8
	13	9	16

In one or two instances improvement was noted whilst the patient was taking the larger doses of Tofranil, but the final recovery occurred suddenly when the patient had been on a maintenance dose for some weeks and when hope of further improvement had been almost abandoned.

INFLUENCE OF OTHER MENTAL OR PHYSICAL ILLNESS

The question arose as to what extent the results were influenced by the presence of other mental illness or by the presence of physical disability in the subjects of the trial.

The findings are tabulated below and the importance of their bearing on the results was ascertained by chi-squared.

Result	Mental Illness Complicating Depression		
Good	..	..	None
Fair	..	..	Paraphrenia
			Schizophrenia
Poor	..	..	Demented
			Schizophrenia
			Inadequate
			Personality

$$\chi^2 = 7.3 \text{ (Significant at a } 0.05 \text{ level)}$$

The physical conditions considered were hypertension, marked arteriosclerosis, cardiac disease and anaemia.

Result	Number Suffering from Physical Disability
Good	5
Fair	8
Poor	8

$$\chi^2 = 1.8$$

Thus in this series the chances of a good recovery were prejudiced by the presence of mental illness other than depression, but were not significantly affected by the presence of cardio-vascular disease or anaemia.

DURATION OF HOSPITALIZATION

Considerable pressure is exerted on the part of patients and their relatives in favour of short-term treatment.

If Tofranil is to provide an alternative to E.C.T. in the treatment of depression the question of duration of hospitalization is important. The average length of stay in hospital for those who received Tofranil from the outset was 12.1/3 weeks. This period was rather longer than that required for the recovery of patients receiving E.C.T. alone, but there is some evidence that the prolongation was in part due to physical conditions.

OUT-PATIENTS

A study was also made of twenty-one out-patients suffering from relatively mild conditions of depression. A controlled technique was used for twelve of these, but was abandoned because in practically every case it was easily apparent which patient had had Tofranil and which the placebo. Those receiving the placebo showed no improvement. Of those taking Tofranil four showed no improvement and of these three were neurotic and the other had an inadequate personality whilst three did not persevere with treatment.

Of the fourteen patients who did well one suffered from reactive depression, three from endogenous depression and ten from involutional melancholia.

The ages varied between 32 years and 76 years and the doses of Tofranil used ranged from 50 mg. t.d.s. to 75 mg. t.d.s.

One patient who recovered rapidly from her depression had been ill for twelve months and during that time most of the anti-depressant drugs and some of the tranquillizers had been prescribed with little effect. There was an exacerbation of symptoms when this patient was taking the placebo, but a rapid response when Tofranil was given.

SIDE-EFFECTS

1. Dryness of the mouth was a very common complaint and in two cases this led to a stomatitis progressing in one of these to a parotitis.
2. Sweating was complained of by about one-third of the cases treated.
3. Transitory loss of power in limbs was complained of by two neurotic patients.
4. Rashes developed in two patients and in both cases subsided without withdrawal of the drug.
5. Trembling of hands was noticed frequently in the older patients.
6. Acute mania of sudden onset and sudden subsidence and lasting about twelve hours occurred in one patient.
7. A feeling of remoteness and detachment was complained of in a few instances.
8. The blood-pressure appeared to be little affected.
9. Dizziness was a relatively rare complaint.
10. Two cases of gastro-enteritis may have been attributable to Tofranil.

SUMMARY

A trial of imipramine was made using a controlled technique with forty in-patients suffering from morbid depression. The results were ascertained by chi-squared and demonstrated a definite improvement in those patients taking Tofranil.

A second study was made of twenty-one out patients suffering from moderately severe conditions of depression. On clinical assessment relief from depression was found to have occurred in a number of patients who received Tofranil but no improvement occurred in those taking the placebo.

There were indications that in some cases significant improvement did not occur until late in the course of treatment.

Results were not good when the depression was complicated by other mental illness, but appeared unaffected in the presence of anaemia or cardiovascular disease.

Side-effects were variable but the most important were dryness of the mouth stomatitis and parotitis and probably gastro-enteritis.

This trial series ended in September, 1959, and only one patient who received Tofranil alone returned to hospital with a recurrence of depression in the subsequent four months.

IMIPRAMINE IN CHRONIC DEPRESSION

By

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IMIPRAMINE hydrochloride (N-(γ -dimethylaminopropyl)-iminodibenzyl hydrochloride, "Tofranil") has been shown by many investigators to be of value in the treatment of depressive states. The reports of Kuhn (1957, 1958) and of Kielholz and Battegay (1958) have been followed by confirmatory papers from other authors. A number of contributors to the McGill University Symposium on Depression and Allied States (1959) commented favourably on the value of imipramine in depression; Hoff, however, while agreeing that the drug is useful in acute depressions stated that he found it ineffective in chronic depression.

In Britain, Ball and Kiloh (1959) have carried out a controlled trial of imipramine in out-patients suffering from depression. They found a statistically significant response, compared with the effect of placebo tablets, in both endogenous and reactive depressions. Another trial has been reported by Leyburg and Denmark (1959). These workers treated 74 patients with depressive states and 28 per cent. made a complete recovery. The authors concluded that "the further trial of this promising drug should at this stage be primarily concerned with the chronic depressive patients of whom many remain institutionalized at present".

This paper reports the results of such a trial. The investigation was undertaken to obtain information concerning the value of imipramine in patients with long-standing depression which had been resistant to other treatments. All the patients studied had been ill for at least one year, most of them for much longer. The trial was designed as a careful clinical study of a small group of patients. The pattern of the illness was in each case well established and most of the patients had had several previous treatments under similar conditions without improvement. It seemed unlikely therefore that the mere act of presenting another new tablet would in itself bring about recovery. The study, including follow-up, has been conducted over a period of thirteen months.

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MATERIAL

Thirty-three patients were selected for study. All had been continuously depressed for at least one year.

The diagnoses were:

Endogenous depression	..	..	..	..	..	26
Personality disorder with depression	..	..	..	..	..	4
Paranoid state with depression	..	..	..	..	..	1
Cerebral arteriosclerosis with depression	..	..	..	..	..	2

Depression was the dominant symptom in all the patients.

The average duration of illness was 4.6 years (range 1 to 11), the average age 64.5 years (range 48 to 83). There were 27 females and 6 males.

All but 6 patients had had electroplexy (E.C.T.), usually several courses, but in none had the response been satisfactory. In the other six E.C.T. had been withheld because of cerebral arteriosclerosis or advanced age. In addition, 17 of the patients had had phenothiazine derivatives, 2 amphetamine, 2 iproniazid and 2 benactyzine—all without response.

METHODS

Imipramine was given by mouth in three doses per day, the total daily dose being:

1st and 2nd days	..	..	..	..	..	100 mg.
3rd day	..	..	..	..	..	150 mg.
4th day	..	..	..	..	..	200 mg.
5th day	..	..	..	..	..	250 mg.
6th and subsequent days			..	..	..	300 mg.

Three hundred mg. daily was then administered until improvement began or—as happened frequently—side-effects dictated a reduction in dose. In three of the earlier cases a change to injection treatment was made when, after four weeks, there had been no improvement. This change was not made in later cases, as injections appeared to offer no advantage over oral administration of the drug. Imipramine was given for at least six weeks before the trial was abandoned as a failure, except in two cases. (One of these, the only one in the series with a paranoid state and depression, became so agitated and distressed that imipramine was discontinued after 17 days. The other, a man with an endogenous depression, complained bitterly of a tremulous sensation in the abdomen and became so agitated that the drug was stopped after 21 days.) No other anti-depressant treatment (E.C.T. or mono-amine oxidase inhibitors) was given to any of the patients during the trial.

In each case the mental state was assessed by frequent clinical interviews and no improvement was recorded unless there was an unequivocal amelioration of the depressive symptoms. All patients were finally assessed at the beginning of March, 1960 (9–13 months after the start of treatment), except those previously excluded from the trial because of failure to respond. In general, patients recovering were kept on a maintenance dose of imipramine of 50–100 mg. per day.

RESULTS

Seven patients (21 per cent.) made a complete recovery, one after a period of hypomania. At the time of assessment all these had been discharged from

hospital. In a further 8 patients (24 per cent.) there was a definite improvement. Two of these had been discharged home at the time of assessment. Eighteen patients (55 per cent.) showed no sustained response although in 3 of them there was transient improvement (lasting respectively 11, 6 and 2 months before relapse occurred). Four of these 18 developed transient hypomanic states during treatment.

One of these latter four, a woman who had been given several courses of E.C.T. without sustained improvement before the start of the trial, became elated after three weeks on imipramine. Seven weeks later she was symptom free and was discharged home on a maintenance dose. She remained well for nine months but then became depressed again. Increasing the dose of imipramine to 300 mg. daily was of no avail and she required re-admission to hospital. Another patient became hypomanic after eight weeks on imipramine. Although the drug was discontinued immediately, the hypomania took five months to subside. The patient was well for one month after this but she then became depressed again and this time did not respond to imipramine. A third patient became hypomanic in the ninth week of treatment; she rapidly entered a state of manic stupor which was only terminated by E.C.T. (After a few weeks of normal affect she once more became depressed but it was not considered advisable to start imipramine again.) The fourth patient responded well to imipramine at first, but became mildly elated after six months on the drug. During the next month the hypomania increased in severity and chlorpromazine was substituted for imipramine. This was followed (2½ months later) by a return of depression; imipramine was recommenced and two weeks later, at the end of the trial, the patient was once more improving.

At the time of final assessment 19 patients had been changed to other treatments because of unsatisfactory response to imipramine.

SIDE-EFFECTS

The incidence of side-effects complained of spontaneously was:

Tremor	..	..	..	..	..	..	..	24
"Dizziness" and "giddiness"	..	..	..	..	..	..	..	10
Dry mouth	..	..	..	..	..	..	..	7
Flushing of skin	..	..	..	..	..	..	..	4
Increased agitation	..	..	..	..	..	..	..	4
Hyperhidrosis	..	..	..	..	..	..	..	3
Blurring of vision	..	..	..	..	..	..	..	2
Deafness (transient)	..	..	..	..	..	..	..	2
Dysarthria	..	..	..	..	..	..	..	1

There were no significant variations in blood pressure.

The most troublesome side-effect, apart from hypomania, was a fine tremor affecting most commonly the upper limbs and in some cases the lower limbs and trunk; it was present equally at rest and during voluntary movement and was not accompanied by any extra-pyramidal signs. It occurred in 73 per cent. of cases, and often necessitated reduction in dosage. In one case it was very severe indeed, affecting the whole body and persisting while the patient was asleep at night; orphenadrine 300 mg. daily did not lessen the tremor which only disappeared when imipramine was withdrawn.

Two patients (aged 57 and 78) fell and sustained fractured femurs while on imipramine. Two others developed ulceration of the mouth but white cell

counts were normal. This latter complication was probably secondary to dryness of the mouth and disappeared with simple local treatment despite continuation of imipramine therapy.

DISCUSSION

Our "complete recovery" rate of 21 per cent. is similar to the 28 per cent. reported by Leyberg and Denmark, and we feel it is encouraging in view of the long-standing and previously intractable nature of the cases treated. Response was best in the endogenous depressions, all the complete recoveries occurring in this group.

The development of hypomania during the administration of imipramine has been mentioned by Kielholz and Battegay (1958), Delay and Deniker (1959), Berthiaume (1959), Leyberg and Denmark (1959) and others. It is, perhaps, of interest to note that only two of our five patients had previously shown any evidence of hypomania, and in each of these it had been limited to a brief spell following E.C.T. The other three had been continuously depressed for three, five and ten years respectively without ever showing signs of hypomania. Two of these patients showed a mixed affective picture as depression gave way to hypomania.

For the most part side-effects were troublesome rather than serious. Foster and Lancaster (1959), however, have drawn attention to the incidence of disturbance of motor function during imipramine therapy. They report nine patients, three of whom fell and sustained fractures. It seems likely, therefore, that imipramine treatment may have been a contributory factor in the fractures occurring in two of our patients. One of these, however, (a 78-year old woman) was on a maintenance dose of only 25 mg. b.d. when she sustained her injury. Falls, and consequent fractures, are a definite hazard of imipramine therapy and a cautious dosage schedule is probably advisable, especially in the elderly. We now feel that the maximum dose used in this trial (300 mg. daily) is higher than is usually necessary. Two hundred-225 mg. daily is probably adequate in most cases, and in old people it may well be wiser not to exceed 150 mg. daily.

It has been our policy to keep patients responding to imipramine on a small maintenance dose, but in one patient the drug has been discontinued without ill-effect. On the other hand, two patients relapsed while on maintenance therapy. In two other cases there was a transient return of symptoms which disappeared when the maintenance dose was increased. It seems that a period of several months at least should be covered by maintenance treatment in such long-term cases as those reported here.

SUMMARY

1. Thirty-three long-standing, previously intractable cases of depression were treated with imipramine.
2. Seven patients (21 per cent.) made a complete recovery, and a further 8 (24 per cent.) showed a definite improvement.
3. Five patients developed hypomania during treatment.
4. Disturbance of motor function was common, and two patients sustained fractured femurs. Reduced dosage and careful supervision are required when imipramine is administered to elderly patients.

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A PSYCHOMETRIC ASSESSMENT OF THE EFFECTS OF IMIPRAMINE

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INTRODUCTION AND METHOD

THE clinical evaluation of a controlled investigation of the effects of Tofranil as an anti-depressant is described elsewhere (Holdway, 1960). This paper describes psychological assessments on the same in-patient sample.

The following measures were obtained before treatment (drug or placebo) and repeated after fourteen days:

1. *Coloured Progressive Matrices*

A measure of non-verbal intellectual performance (Raven, 1956, revised edition).

2. *Mill Hill Vocabulary Scale* (Oral Definitions Form)

A measure of verbal intellectual performance (Raven, 1958, revised edition).

3. *The Objective Rorschach*

Here, the subject selects two responses from a list of twelve given for each of the ten Rorschach cards. From the original standardization, four of these responses are "normal", four are "neurotic", and four are "psychotic". "Normal" choices are arbitrarily scored 1, "neurotic" 2 and "psychotic" (or omitted) choices, 3. The possible range of scores is, therefore, 20-60. This method was found to give significant differences between groups of normals, neurotics and psychotics (O'Reilly, 1956) and to be also sensitive to response to therapy (O'Reilly, 1955).

4. *The Maudsley Personality Inventory*

This has scales measuring the relatively independent "dimensions" of neuroticism and extraversion. The short form was finally used (Jensen, 1958) as the standard form proved to be too long for the type of patient studied.

Table I indicates the mean scores and standard deviations for drug and placebo groups before and after treatment on these measures.

First, let us consider the scores of both groups before treatment. On non-verbal and verbal intelligence tests, the average ability in both cases is in the lower reaches of the average range. With regard to the Objective Rorschach score, O'Reilly (op. cit.) from his data, says any score above 37 is "almost certainly psychotic". Both groups are above this figure. With regard to neuroticism, both groups are nearer to normal group performances rather than neurotic groups (Jensen, 1958). On the extraversion scale, there is for the first time an apparently significant difference between the two groups. The placebo

TABLE I

Variable						Tofranil Group (N 19)		Placebo Group (N 17)	
						Mean	S.D.	Mean	S.D.
Matrices	(1)	..	..	..	..	18.4	9.6	18.5	8.9
	(2)	..	..	..	..	20.5	6.4	15.9	4.7
Mill Hill Vocabulary Scale	(1)	..	..	..	..	37.7	12.3	37.7	7.9
	(2)	..	..	..	..	40.4	14.4	39.6	8.9
Objective Rorschach	(1)	..	..	..	..	39.5	8.8	39.3	8.0
	(2)	..	..	..	..	36.3	7.4	39.2	8.8
Maudsley Personality Inventory Neuroticism	(1)	..	..	..	..	6.1	3.0	7.5	2.8
	(2)	..	..	..	..	4.5	2.8	4.5	2.9
Maudsley Personality Inventory Extraversion	(1)	..	..	..	..	4.9	2.7	6.9	2.6
	(2)	..	..	..	..	6.1	2.8	7.2	3.0

N.B.: (1) before treatment; (2) after treatment.

group is more extraverted than the Tofranil group ($t=2.119$, $S\ 0.05$). Even so, both groups are less extraverted than normal groups.

Generally speaking, the two groups (as would be expected from their random selection) are similar before treatment. On all tests except the M.P.I. their scores are practically identical. Perhaps the small possible range of scores on the M.P.I. Short Forms accounts for the greater variability on its measures rather than a real difference between the groups.

It would seem then, that both groups are of average intelligence, not neurotic, possibly slightly introverted, but clearly psychotic, according to test performances.

Secondly, a comparison of changes in performance in the two groups before and after treatment:

1. Coloured Matrices

From Table I it can be seen that the Tofranil group improved their performance, whereas the placebo group deteriorated. This difference just fails to be statistically significant ($t=1.946$). Non-verbal performance tends to be impaired in mental illness, particularly when this is of psychotic dimensions. The trend here suggests some improvement with Tofranil, but a worsening with placebo.

2. Vocabulary

Both groups improve their score, particularly the Tofranil group. This latter improvement just fails to be significant at a statistical level ($t=1.908$). That there is some improvement in both groups indicates the social factors involved in an oral vocabulary test, which will be of importance in discussing the M.P.I. findings.

3. Objective Rorschach

Here, the Tofranil group improve, whereas the placebo group remain stationary. The placebo group is, therefore, still as psychotic, whereas the Tofranil group has improved. It must be noted, however, that their score is still abnormal and that the improvement does not become statistically significant ($t=1.120$).

4. *M.P.I. Neuroticism*

Both groups become less neurotic than normals after treatment. In the placebo group this is highly significant ($t=6.137$, $S\ 0.01$) but less so in the Tofranil group ($t=1.606$). As, however, their scores are, in fact, identical after treatment, their original differences, as suggested, are probably chance differences connected with the short possible range of the test. The decrease, however, in neuroticism, in both groups, probably reflects (a) the effects of being in hospital undergoing treatment, and possibly (b) desire after treatment to leave hospital.

5. *M.P.I. Extraversion*

Both groups become slightly more extraverted. The reasons for this are probably similar to the above decreases in neuroticism.

CONCLUSIONS

Although statistical significance is inevitably affected by the shortness of the therapeutic trial period, the psychological assessments seem to be quite clear in their indications. First, both Tofranil and placebo groups show similar trends on those tests involving social and neurotic factors. Secondly, on measures sensitive to the degree of psychoticism Tofranil has a therapeutic effect, completely absent in the placebo group. These findings, therefore, support those of Holdway (op. cit.).

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ETHINAMATE AND METHYPRYLONE AS HYPNOTICS: A COMPARATIVE TRIAL

By

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THE use of barbiturates in the treatment of insomnia carries a constant risk of habituation and of fatal poisoning from suicidal or accidental overdose. For these reasons, new non-barbiturate hypnotics deserve the closest attention. Ethinamate ("Valmidate") and methyprylone ("Noludar") are two such drugs. No trial comparing the hypnotic efficacy of ethinamate with a barbiturate has yet been reported, though Gruber *et al.* (1954) found the day-time sedative effect of 500 mg. ethinamate to be less (in duration of action) than 100 mg. of quinalbarbitone sodium. Methyprylone has been compared with barbiturate by Stewart (1956) who found 200 mg. equivalent to 100 mg. of amylo- or butobarbitone, by Lasagna (1956) who found 250 mg. equivalent to 100 mg. of pentobarbitone, and by Thomson (1958) who found 400 mg. equivalent to 100 mg. of quinalbarbitone.

The present paper reports a clinical trial designed to compare the hypnotic efficacy of ethinamate and methyprylone against each other and against butobarbitone and a placebo. The method used has yielded consistent and therefore probably reliable results in previous trials (Hare, 1955; Salter *et al.*, 1959).

METHOD

Subjects. The subjects were 47 patients suffering from neurotic or recent psychotic illness, all in good physical health and all complaining of some degree of insomnia. Seven patients failed to complete the minimum of twelve nights on the trial. Of the remaining 40 patients, 18 (11 male, 7 female) were in the Maudsley Hospital and 22 (8 male, 14 female) in Bethlem. Their ages ranged from 17 to 70 years, with a mean of 38.

Drugs. The comparison was made between butobarbitone 200 mg., methyprylone 200 mg., ethinamate 500 mg. and a lactose placebo (to which quinine was added to simulate the taste of barbiturate). The drugs were put up in identically-appearing capsules and administered in a randomized order (different in the two hospitals) over a nearly consecutive series of nights. The randomization was so designed that each patient received each drug four times during a series of 16 nights and on any one night the different drugs were, as far as possible, equally distributed among the patients. In the Maudsley Hospital the patients swallowed the capsules whole but in Bethlem the capsules

were emptied into water and taken as a draught. The four drugs were identified by letters and the code known only to the pharmacists until the conclusion of the trial.

Records. The drugs were given at the same hour (9.30 p.m.) each night. At half-hourly intervals until 6.30 a.m. the night nurse visited each patient and recorded whether he was awake or asleep. The nurse also recorded whether the patient's sleep had been quiet or restless and noted any spontaneous comments by the patients on the quality of his sleep or his condition on waking. If a patient was awake between periods of sleep, this was counted as a night of "interrupted sleep".

A total of 976 nights were recorded, the average number of nights per patient being 24, with a range of 13 to 44.

RESULTS

For comparative purposes, the principal measure of a patient's response to a drug was taken as the mean number of times per night on which he was recorded as being awake. This number, multiplied by 30, will approximately represent the time in minutes for which he was awake during the nine hours recorded. The time taken to fall asleep may be represented in a similar way. Table I shows the combined results for the 40 patients. Correlated t-tests

TABLE I
Sleep Record on Different Drugs, 40 Patients

Sleep Index	Drugs			Lactose
	Buto- barbitone 200 mg.	Methy- prylone 200 mg.	Ethin- amate 500 mg.	
Mean time awake (minutes per patient per night)	95	110	120	128
Mean time to fall asleep (minutes per patient per night)	44	51	50	51
Interrupted sleep (number of nights when this occurred)	54	81	80	86
Restless sleep (number of nights so reported)	26	36	36	32

between the mean times awake on the different drugs give the following results. Butobarbitone is significantly better, i.e. is associated with a shorter time awake, than each of the other drugs ($P < 1$ per cent.); methypylone is significantly better than the placebo ($P < 1$ per cent.); the differences between methypylone and ethinamate and between ethinamate and the placebo do not quite reach the 5 per cent. level of significance. The butobarbitone scores are also significantly better than the other drugs for the mean time to fall asleep and for the number of nights of interrupted sleep ($P < 5$ per cent.).

Table II shows the effect of different factors on the comparative scores for the mean time awake. It can be seen that none of the four factors examined had any appreciable influence on the relative efficacy of the drugs.

No adverse comments or complaints of hangover were recorded during the trial.

TABLE II

Mean Time Awake on Different Drugs (Lactose Expressed as 100) by Various Factors

Factor				Number of Patients	Drugs			Lactose
					Buto- barbitone 200 mg.	Methy- prylone 200 mg.	Ethin- amate 500 mg.	
Hospital:								
Maudsley	..	..	18	76	85	89	100	
Bethlem	..	..	22	74	87	98	100	
Sex:								
Male	..	..	19	75	84	91	100	
Female	..	..	21	72	87	97	100	
Age:								
Under 35	..	..	20	72	82	88	100	
Over 35	..	..	20	78	91	102	100	
Diagnosis:								
Depression	..	..	24	82	94	102	100	
Not depression		..	16	65	77	85	100	
All patients	..	..	40	74	86	94	100	

DISCUSSION

In terms of the indices used, the results indicate that butobarbitone 200 mg. is a more effective hypnotic than either methylprylone 200 mg. or ethinamate 500 mg. This is in line with the findings of Stewart (1956) that methyprylone 200 mg. is about as effective as butobarbitone 100 mg. In contrast, Thomson (1958), using the method of sequential analysis, found no significant difference between methyprylone 200 mg. and placebo, although 400 mg. produced a significantly better result. It may be, however, that his method, based on the patients' subjective preferences, provides a less clear distinction between the actions of weak hypnotics and placebos.

Ethinamate, in the present study, showed a hypnotic action no better than the placebo, a finding which is in agreement with Gruber *et al.*

It is of interest that butobarbitone caused a significantly more rapid onset of sleep than did the other drugs, for ethinamate and methyprylone are marketed as rapidly acting hypnotics, whereas butobarbitone is classed as a hypnotic of "medium duration". The work of Lasagna (1956) has already thrown doubt on the common supposition that, for clinical purposes, the barbiturate hypnotics can be classed into short-, medium- and long-acting.

Our finding that the comparative efficacy of the drugs was uninfluenced by age or sex is in accordance with that of Drew (1958), who found no relation between these factors and the response to alcohol as measured by driving-test errors.

The differences we observed between the active drugs and the placebo cannot be expressed in absolute terms. The patients received the placebo on only one night in four and it seems likely that the rhythm of satisfactory sleep established by three nights on active drugs would be to some extent carried over to the fourth night, thus increasing the apparent efficacy of the placebo. Indeed, the use of a placebo in this type of comparative trial is probably unnecessary.

SUMMARY

1. By a controlled clinical trial, the hypnotic efficacy of ethinamate ("Valmidate") and methyprylone ("Noludar") were compared with each other and with butobarbitone and a placebo. The subjects were 40 psychiatric patients and an average of 24 nights sleep per patient was objectively recorded.

2. The trial was divided between two hospitals, with consistent results.

3. Butobarbitone 200 mg. was significantly more effective than the other drugs on most of the criteria used, and this comparative efficacy was uninfluenced by factors of age, sex or diagnosis.

4. Methyprylone 200 mg. was more effective than the placebo, but did not differ significantly from ethinamate 500 mg. Ethinamate 500 mg. was not significantly more effective than the placebo.

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A CONTROLLED TRIAL OF HALOPERIDOL IN CHRONIC SCHIZOPHRENICS

By

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4-P-CHLOROPHENYL-1-(3-p-fluorobenzoylpropyl)-4-hydroxypiperidine (R.1625, Haloperidol) is a new compound synthesized by Janssen *et al.* (1959) and reported to have biological properties similar to those of the phenothiazines at a much lower dosage level. One difference, however, was a greater tendency to potentiate pentobarbitone hypnosis. Von Eiff and Jesdinsky (1960) conducted a "double blind" trial in 28 normal subjects using 4 mg. Haloperidol 2½ or 4½ hours before the experimental period. Subjective effects included fatigue or fatigue and agitation in females. The drug did not appear to influence intellectual function as tested, but reduced self-criticism. There were minor cardio-vascular effects and a tendency to fatigue in ergometry performances. A number of clinical reports have appeared (Divry *et al.*, 1960; Delay *et al.*, 1960) suggesting that Haloperidol is of value in psychomotor agitation and especially in mania in doses of 2–15 mg. daily. Gerle (1960) reports favourably on the drug in schizophrenic patients. Most authors note a high incidence of pseudo-Parkinsonian side-effects (40–80 per cent. of cases) and a section of a recent symposium on the drug in Belgium was devoted to "neurodysleptic syndromes" (dystonic reactions, oculogyric crises, etc.) produced by it. Pichot (1960) at the symposium reported that these reactions can be controlled by chlorpromazine.

OBJECTS OF STUDY

It was decided, in the light of the information above, to design a trial which might show whether:

1. Haloperidol is therapeutically useful in chronic schizophrenics.
2. Haloperidol is therapeutically useful in any particular sub-group of such patients.
3. Haloperidol is of any value in the treatment of any symptom or symptom-complex in such patients.
4. The therapeutic properties are adversely affected by a slow build-up to the anticipated therapeutic dose.
5. Side-effects are lessened by a slow build-up to the anticipated therapeutic dose.
6. Chlorpromazine or other phenothiazines can protect against side-effects.

METHOD

Twenty withdrawn chronic schizophrenic patients in a group of long-stay wards were selected for the trial (Table I) and divided into four groups (1, 2, 3 and 4) of five patients each by the senior investigator. The patients allocated

TABLE I
General Data of Twenty Schizophrenic Patients

Number	Age	Previous Treatment	Duration of Illness in Years	Diagnosis
1	31	Prochlorperazine	11	Catatonic schizophrenia
2	36	Prochlorperazine	13	Hebephrenic schizophrenia
3	41	Prochlorperazine	22	Catatonic schizophrenia
4	39	Prochlorperazine	15	Hebephrenic schizophrenia
5	39	Prochlorperazine	22	Catatonic schizophrenia
6	32	Chlorpromazine	11	Paranoid schizophrenia
7	61	Chlorpromazine	23	Catatonic schizophrenia
8	22	Chlorpromazine	3	Hebephrenic schizophrenia
9	27	Chlorpromazine	7	Catatonic schizophrenia
10	36	Chlorpromazine	13	Catatonic schizophrenia
11	39	Reserpine	15	Simple schizophrenia
12	67	Chlorpromazine	23	Catatonic schizophrenia
13	39	Reserpine	12	Catatonic schizophrenia
14	54	Nil	18	Hebephrenic schizophrenia
15	55	Nil	12	Simple schizophrenia
16	57	Nil	26	Catatonic schizophrenia
17	56	Nil	23	Catatonic schizophrenia
18	59	Nil	23	Hebephrenic schizophrenia
19	31	Nil	8	Hebephrenic schizophrenia
20	46	Nil	21	Paranoid schizophrenia

to group 1 were all receiving prochlorperazine at the start of the trial; Group 3 were all receiving chlorpromazine; Group 2 were not receiving drugs of any kind; Group 4 consisted of the remainder and included two patients receiving reserpine and one chlorpromazine. The senior investigator controlled the prescription of drug and placebo in a "double blind" cross-over design. As far as doses were concerned, two schedules were employed which predetermined a maximum rise each week. If the patient's clinical condition was satisfactory, or, alternatively, toxic manifestations were observed, then the doses could be adjusted below the permitted maximum. The schedules were designed to give a slow build-up of dose ("low dosage schedule") and a more rapid build-up ("high dosage schedule").

The low dosage schedule permitted, using 3 mg. tablets:

- $\frac{1}{4}$ tablet b.d. for 2 days
- $\frac{1}{2}$ tablet b.d. for 2 days
- $\frac{1}{2}$ tablet t.d. for 3 days
- 1 tablet b.d. for 7 days
- 1 tablet t.d. for 7 days

Free prescribing up to 8 tablets daily for 7 days.

This phase thus occupied four weeks.

The high dosage schedule permitted:

1 tablet b.d. for 7 days

1 tablet t.d. for 7 days

Free prescribing up to 8 tablets daily for 14 days.

This phase also, therefore, occupied four weeks.

Patients in Group 1 were started on the low dosage schedule of the drug, Group 3 were started on the high dosage schedule of the drug. The drug was thus employed after courses of treatment with prochlorperazine and chlorpromazine respectively. Groups 2 and 4 received placebo tablets in high and low doses respectively. At the end of a month all drug treated patients were changed to placebo without warning the staff, by simply substituting inert tablets and using the same labelling, etc. At the end of a further month the patients on Groups 1 and 3 were again treated with the drug at the last dose with which they had previously been treated. Those patients treated with placebo in the first month (Groups 2 and 4) were treated with the drug in the second month on high and low dosage schedules. In the third period they were put back on placebo without warning by simple substitution (Table II). The trial was terminated in this form after ten weeks.

TABLE II
Design of Trial

	Group	1	2	3	4
1st 4 week period		A	B	C	D
2nd 4 week period		BA	C	DC	A
Final 2 week period		EA	DC	FC	BA

Group 1—Prochlorperazine treatment up to trial

Group 2—No drugs up to trial

Group 3—Chlorpromazine treatment up to trial

Group 4—Various treatments up to trial

A — Low dosage schedule—drug

B — Low dosage schedule—placebo

C — High dosage schedule—drug

D — High dosage schedule—placebo

BA — Placebo in last dose of A

DC — Placebo in last dose of C

EA — Drug in last dose of A

FC — Drug in last dose of C

Ratings were performed weekly by the second investigator and by the senior nursing staff using a standard interview technique (Baker and Thorpe, 1956) and a behaviour rating scale (Baker and Thorpe, 1956) respectively. In the latter case in order to restrict the ratings to personal observations, time sampling was employed and the nurses were asked to restrict their scoring to a set day each week when they were on duty. Not only were none of the raters aware of active and placebo treatment periods, but, in fact, they were also completely unaware of the true design of the trial. Before the study started they had been asked to pick ten matched pairs of patients for a concurrent study of *two* drugs. In each pair they were told one patient would receive one of the drugs and the second patient the other. Literature was issued showing the drugs to be similar in action and side-effects—and these were stressed. It was explained that there would possibly be quantitative advantages for one drug *vis-à-vis* the second. The objects of this deception were to prevent generalization from the recognition of side-effects by the raters and maintain the level of observer interest even if the drug were recognized. If side-effects reveal the drug

in a drug-placebo design then clearly many advantages in a double-blind procedure are lost. If side-effects were recognized in this trial they would not mean to the raters that the patient was having something as opposed to nothing. Indeed, side-effects might be noticed in each of the groups that the raters had constructed because both these groups contained patients on the drug. If the raters tended to generalize from their observations they would pass advantages or disadvantages within the two groups they imagined were in use. These groups, in reality, contained random selections of drug and placebo patients because the real groups were chosen on entirely different criteria and thus advantages or disadvantages would go in a random fashion to drug and placebo.

Further information was obtained by a joint examination by both authors, at monthly intervals, to elicit symptoms and from the statutory ward report books in which the nursing staff were encouraged to note anything unusual from day to day.

RESULTS

The nurses' behaviour ratings (Table III) show no inter-group differences which can be considered significant. If Groups 1 and 3, and 2 and 4, are considered together respectively, as patients previously treated and not previously treated with phenothiazines, then the nurses' rating shows an intra-group difference in phenothiazine-treated patients in the last fortnight of the trial as compared with the previous period on placebo ($n=9$: $t=3.1$: $p=<0.05$). The doctor's standard interview scores (Table IV) show a number of inter-group differences which achieve accepted levels of significance. Comparing all drug-treated with all placebo-treated patients in the first week of the trial and in the fourth week of the trial (for $n=18$: $t=2.2$ and 2.45 respectively $p=<0.05$) there is a reduction of scores favouring the drug. There is a similar result in the tenth week of the trial ($n=18$: $t=2.1$: $p=<0.05$). Thus in patients previously treated with phenothiazines three of six comparisons show a significant reduction favouring the drug. In patients not previously treated there are no significant differences. Making intra-group comparisons, patients previously treated with phenothiazines show a significant reduction in mean scores for the standard interview, comparing the second month with the first month of the trial ($n=9$: $t=2.7$: $p=<0.05$), and also comparing the last fortnight with the first month ($n=9$: $t=3.1$: $p=<0.05$). In patients not previously treated there are no differences. Apart from any effect that the drug may have, it is possible that previously treated patients are those most capable of interaction with environment, and the intra-group changes are, in part at least, a training effect.

As far as the joint interview is concerned the symptom scores are shown in Table V at the start of the trial and at 4, 8 and 10 weeks. Symptoms were rated on a three-point scale, and the check list of symptoms used is given in Appendix A. Toxic symptoms were scored separately and these are shown in parenthesis. No significant differences could be shown between the reductions effected by drug and placebo in the symptoms of illness.

The ward reports were analysed by counting the number of reports of the various incidents or complaints that appeared in drug and placebo periods (Table VI). Trends to increased restlessness and decreased nocturnal incontinence and aggressiveness were noted with the drug. On the other hand there was a marked increase in reports of pallor, drowsiness, fatigue, tremors and other parkinsonian and dystonic symptoms with the drug.

TABLE III
Results of Nurses' Behaviour, Rating Scale: Mean Reduction of Scores and S.D.s

Week	1	2	3	4	5	6	7	8	9	10
Group 1 ..	3.2 ± 3.31	0.8 ± 2.48	1.8 ± 3.43	3.0 ± 1.67	1.6 ± 2.04	0.6 ± 1.62	1.6 ± 4.13	3.0 ± 1.90	3.0 ± 0.9	6.2 ± 2.64
Group 3 ..	6.4 ± 3.72	1.0 ± 3.1	2.0 ± 4.05	5.4 ± 5.00	1.8 ± 5.84	-2.0 ± 4.59	4.2 ± 5.19	0 ± 5.52	0.5 ± 1.5	7.0 ± 3.8
Groups 1 and 3 ..	4.8 ± 3.47	0.9 ± 2.84	1.9 ± 3.75	4.2 ± 3.92	1.7 ± 4.39	-0.55 ± 3.51	2.9 ± 4.86	1.5 ± 4.39	1.9 ± 1.73	6.6 ± 3.12
Group 2 ..	0.4 ± 4.22	0.6 ± 2.52	1.6 ± 1.49	5.8 ± 3.54	1.8 ± 2.23	1.2 ± 3.31	5.0 ± 2.61	1.8 ± 2.04	1.0 ± 0.9	5.6 ± 3.6
Group 4 ..	1.6 ± 6.02	-0.2 ± 2.56	1.2 ± 2.18	6.2 ± 3.49	0.8 ± 4.83	-0.8 ± 2.4	5.8 ± 3.06	1.4 ± 3.72	0.6 ± 4.41	3.4 ± 3.26
Groups 2 and 4 ..	1.0 ± 5.24	0.2 ± 2.52	1.4 ± 1.88	6.0 ± 3.53	1.3 ± 3.80	0.2 ± 3.06	5.4 ± 2.87	1.6 ± 2.99	0.8 ± 3.18	4.5 ± 3.6

TABLE IV
Results of Standard Interview: Mean Reduction of Scores and S.D.s

Week	1	2	3	4	5	6	7	8	9	10
Group 1 ..	1.2 ± 0.9	1.8 ± 1.28	1.4 ± 1.39	2.5 ± 1.48	2.9 ± 1.52	2.6 ± 2.95	3.0 ± 1.38	3.0 ± 0.49	2.7 ± 1.14	2.5 ± 1.23
Group 3 ..	0.9 ± 0.9	0.7 ± 1.47	-0.3 ± 2.89	1.5 ± 1.0	1.5 ± 0.55	1.4 ± 0.77	1.1 ± 0.66	1.6 ± 0.49	1.4 ± 0.44	1.6 ± 0.7
Groups 1 and 3 ..	1.05 ± 0.9	1.25 ± 1.48	0.55 ± 2.38	2.0 ± 1.36	2.2 ± 1.35	2.0 ± 2.40	2.05 ± 1.51	2.3 ± 1.05	2.05 ± 1.09	2.1 ± 1.14
Group 2 ..	-0.4 ± 0.46	1.1 ± 1.24	0.3 ± 1.81	-0.5 ± 1.57	1.4 ± 1.16	1.2 ± 1.75	1.3 ± 1.89	1.7 ± 2.06	0.8 ± 1.52	1.0 ± 1.52
Group 4 ..	-0.9 ± 2.25	1.0 ± 2.15	-1.0 ± 2.80	-0.4 ± 1.63	1.0 ± 2.30	0.6 ± 2.00	0.4 ± 1.93	1.6 ± 1.64	0.4 ± 2.64	0.3 ± 1.90
Groups 2 and 4 ..	-0.65 ± 1.91	1.05 ± 1.75	-0.35 ± 2.46	-0.45 ± 1.60	1.2 ± 1.83	0.9 ± 1.64	0.85 ± 1.96	1.65 ± 1.87	0.6 ± 2.17	0.65 ± 1.76

TABLE V

Symptom Ratings and Side-Effects (in parenthesis) in Twenty Schizophrenic Patients

Week	0	4	8	10
		After Drug	After Placebo	After Drug
Groups 1 and 3	29 (0)	32 (3)	23 (3)	24 (7)
	14 (0)	8 (5)	9 (0)	14 (0)
	22 (0)	18 (2)	22 (0)	20 (0)
	20 (0)	13 (0)	21 (0)	19 (1)
	23 (1)	14 (2)	17 (0)	19 (1)
	13 (0)	6 (2)	13 (0)	5 (0)
	18 (0)	20 (7)	—	19 (7)
	13 (0)	11 (3)	13 (0)	17 (0)
	5 (0)	4 (0)	24 (0)	13 (0)
	16 (0)	16 (0)	11 (0)	17 (2)
		After Placebo	After Drug	After Placebo
Groups 2 and 4	29 (0)	21 (0)	21 (2)	16 (0)
	11 (0)	9 (3)	9 (5)	3 (1)
	20 (1)	14 (0)	15 (0)	19 (0)
	26 (0)	23 (0)	24 (4)	22 (2)
	12 (0)	21 (0)	13 (6)	21 (3)
	18 (0)	19 (1)	19 (8)	20 (0)
	26 (0)	21 (0)	21 (4)	23 (0)
	19 (0)	17 (0)	22 (3)	13 (0)
	21 (0)	23 (1)	31 (3)	21 (0)
	11 (0)	14 (0)	9 (0)	21 (4)

TABLE VI

Analysis of Ward Reports

Symptom or Sign	Drug Period No. of Reports	Placebo Period No. of Reports
Daytime restlessness	147	89
Nocturnal restlessness	43	35
Daytime incontinence	3	2
Nocturnal incontinence	6	23
Dull and retarded	18	22
Bright	21	22
Aggressiveness	7	21
Nocturnal aggression	1	2
Daytime noisiness	5	7
Nocturnal noisiness	3	6
Sleepless	0	3
Pale	34	6
Drowsy	13	2
Vomiting	9	5
Headache	4	0
Anorexia	6	3
Tremors	10	0
Other Parkinsonian and dystonic symptoms	14	0
Feeling ill	3	0
Hair falling	3	0
Getting into bed	23	4
Other toxic symptoms	5	1

A classification of the ward report analysis into the global categories—better, unchanged, worse—showed six patients better on the drug, two unchanged and twelve worse on the drug. The six improved patients owed their improvement to the relief of stupor (2), the control of aggressiveness or

destructiveness (3), and the control of restlessness (1). Of these six four were regarded as catatonic and two as paranoid. Out of eight simple or hebephrenic patients treated none responded, whereas four of ten catatonics responded, as did both paranoids. Diagnostic sub-group evidently plays some part in determining response.

TOXIC EFFECTS

As far as toxic effects are concerned the position is summarized in Table VII.

TABLE VII
Summary of Toxic Symptoms During Trial

Period of Trial	Drug Used Prior to Assessment		Instances of Toxic Symptoms Observed	Cases Treated
At the start of the trial	Prochlorperazine	..	1	5
	Reserpine	..	1	2
	Chlorpromazine	..	0	6
	Nil drugs	..	0	7
At one month	Haloperidol	..	24	10
	Placebo	..	5	10
At eight weeks	Placebo	..	3	9
	Haloperidol	..	35	10
At ten weeks	Haloperidol	..	18	10
	Placebo	..	10	10

It will be seen that 77 instances of toxic symptoms were noted after Haloperidol as against 18 after placebo administration, and of the latter, ten instances were noted only a fortnight after Haloperidol and may thus represent a carry-over effect.

After the low dosage schedule thirty instances of symptoms were noted at one month in ten patients treated. After the high dosage schedule twenty-nine were noted after a month's treatment.

Motor restlessness, variously called "the turbulence phase" and "akathisia", has been observed after the administration of phenothiazines and reserpine and this symptom was examined in the first eight weeks of the trial to see whether it occurred in association with drug administration *per se*, whether it was simply a feature of the schizophrenic process, or finally whether it occurred in association with other signs of drug intoxication. Table VIII demonstrates the

TABLE VIII
Examination of Motor Restlessness and Toxic Signs

					Toxic Signs	No Toxic Signs	Total
No. of restless patients	..	..	..		14	9	23
No. of non-restless patients	..	..	..		5	12	17
Total	..	..	..	..	19	21	40

For $n=1$. $\chi^2=3.9$. $p=<0.05$.

relationship with drug intoxication—the latter having been noted from the joint interview and the motor restlessness from the ward reports respectively. Six patients were reported as restless only while on the drug, and one restless only while on placebo. Eight patients were reported as restless while on drug

and placebo. Three patients had oculogyric crises with or without dystonic phenomena. The first of these had been having reserpine before the trial, was on placebo for a month and was affected after 18 mg. Haloperidol in the high dosage schedule. The second and third patients were treated without incident in the first month in the high dosage schedule, having taken chlorpromazine up to this point. Their reaction occurred after 18 and 24 mg. respectively in a high dosage schedule after a month on placebo. There is no evidence however that other pseudo-Parkinsonian features (tremor, rigidity, etc.) enjoy a protective effect from previous phenothiazine administration. In the first month seven patients were observed with pseudo-Parkinsonian features including one who already showed these features but became worse. Four of these were having chlorpromazine and three prochlorperazine before they started Haloperidol. Eight patients developed similar symptoms having been previously treated with placebo for a month.

CONCLUSIONS

Haloperidol is of limited value in the symptomatic treatment of long-standing schizophrenic patients, and was most effective where the phenothiazines had already been thought to be indicated by the clinicians treating the patients studied. The symptoms affected favourably in the twenty patients concerned were aggressiveness and nocturnal incontinence, but of the six patients who derived most consistent benefit from the drug, two obtained this from the relief of stupor and the others from the control of aggressiveness, destructiveness and restlessness. The diagnostic sub-groups favourably affected were catatonic and paranoid schizophrenia. A slow build-up of the drug to anticipated therapeutic doses does not appear to affect therapeutic properties adversely although overall these were, very limited. On the other hand, side-effects of the pseudo-Parkinsonian type were certainly not lessened by such a build-up.

Oculogyric crises occurred in three patients, all on the high dose schedule and all early in treatment. One of the three had been safely treated with the low dosage schedule previously and two with the high dosage schedule after chlorpromazine. The incidence of this acute side-effect may therefore have some relationship with the rapidity of the build up of the drug, and chlorpromazine may possibly antagonize these effects. Haloperidol is apparently more neurotoxic than chlorpromazine or prochlorperazine, and apart from the pseudo-Parkinsonian and dystonic side-effects produces pallor and drowsiness in a number of patients. A striking side-effect is motor restlessness, which appears to be associated with the appearance of pseudo-Parkinsonism.

The number of patients studied was small, but on the basis of this trial the only reasonable indications for Haloperidol at present seem to be phenothiazine sensitivity (in the toxic sense) or insensitivity (in the therapeutic sense) where the symptomatic picture or diagnosis would normally suggest the use of a phenothiazine drug. Further experience, on the other hand, may show the drug to retain usefulness in lower and less toxic doses than were employed here (up to 18 mg. daily), since some clinical effects have been observed with as little as $1\frac{1}{2}$ mg. daily.

SUMMARY

A double-blind cross-over trial of Haloperidol was conducted on twenty long-stay schizophrenic patients. The results are described in terms of rating scales, symptom responses and diagnosis. Toxic effects of Haloperidol are enumerated and their prevention discussed.

ACKNOWLEDGMENTS

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APPENDIX A

Symptoms and Signs Used in Joint Interview

- | | |
|-----------------------------------|--------------------------------------|
| Abnormal posture. | Systematized delusions—persecutory. |
| Grimaces, tics and mannerisms. | —grandiose. |
| | Non-systematized delusions. |
| Apathy. | Hallucinations—Haptic. |
| Negativism. | —Olfactory. |
| Ambivalence. | —Visual. |
| Automatic obedience. | —Auditory. |
| Thought disorder. | Orientation—for time. |
| Stereotypy. | —and place. |
| Irrelevancies. | Insomnia. |
| Neologisms. | |
| Poverty of ideas. | Cold extremities. |
| Thought blocking. | |
| Autochthonous ideas. | <i>Toxic Signs:</i> |
| Ideas of passivity or influence. | Rigidity. |
| Ideas of reference. | Tremor. |
| Echolalia. | Mask-like face. |
| Pallilalia. | Absence of arm swinging. |
| | Other signs—dystonic phenomena, etc. |
| Blunting or flattening of affect. | |
| Incongruity of affect. | |
| Anxiety. | |
| Depression. | |
| Suspiciousness. | |

IATROGENIC PARKINSONISM*

By

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and

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THERE can hardly be a psychiatrist in this country who has not produced parkinsonism in his schizophrenics with reserpine or phenothiazines: Moore, who was among the first in the field in the use of reserpine, spoke of the parkinsonian syndrome, but there was one observation of his that received only passing attention. This was that a small number of his chronic schizophrenics lost their florid schizophrenic symptoms, to be replaced by a clinical picture that he found closely akin to retarded endogenous depression, to the point of contemplated or attempted suicide.

In our view Moore was on the threshold of a discovery that has at best been exploited by only a few isolated individuals. Our experience of the side-effects of reserpine is negligible, as we administer this in a tablet combined with orphenadrine (Disipal) which obviates them; our hypotheses are based on a study of the phenothiazines, which produce identical side-effects. The motor signs of phenothiazine intolerance, rigidity, tremor, tongue-protrusion, head-rolling, torsion-spasm, oculogyric crises, dystonia and akathisia, are familiar enough, with an incidence of 25 per cent. or more among the active phenothiazines other than chlorpromazine. These manifestations are disturbing, but only to the physician or the patient's relatives. Anyone who has interrogated the patient on his feelings will have appreciated that in general he experiences at worst nothing more than a slight embarrassment that his involuntary movements interrupt the flow of conversation with his physician. He is rarely distressed at his symptom; he is much more likely to be distressed by the onlooker's anguish.

There are 3 ways of dealing with this syndrome; the first is to administer phenothiazines in sufficiently minute doses to preclude the possibility of extra-pyramidal symptoms. This one might call preventive medicine; the second is to reduce the dose if these manifestations appear, and so maybe drop below the therapeutic level; the third is to exhibit an anti-parkinsonian agent. This last procedure is tacitly regarded by many as "going too far", with the result that these never know what they are missing.

Nevertheless it is not with this aspect that we are here concerned.

All present, but perhaps those especially with extensive neurological experience, will be aware of the fact that those patients with the less severe motor manifestations of extra-pyramidal disorder exhibit a mental syndrome consisting of dejection, hopelessness, and apathetic inertia. This applies whether the motor disorder is due to paralysis agitans, encephalitis, cerebrovascular disease, reserpine or phenothiazines. It is our contention that this

* Presented to South-Western Division R.M.P.A. on 21 April, 1960 at Herrison Hospital.

peculiar psychic state, akin as it appears to be to endogenous depression, is an integral part of the extra-pyramidal syndrome. However, this realization did not come to us as a brilliant flash of insight, but rather by the Watsonian method.

We first began by giving Artane or Disipal to those phenothiazine-treated patients who were showing minor extra-pyramidal symptoms. As the motor signs disappeared we observed an increase of psychomotor activity. From this we continued in haphazard way to give one or other of these anti-parkinsonian agents to schizophrenics whose florid symptoms were controlled by phenothiazines, but who were inert and seemingly apathetic. The response was striking, for this state was generally replaced by renewed interest, activity and initiative.

In the course of time many patients were given one of these drugs in addition and we felt that it was time we produced some statistically evaluable evidence.

To this purpose we selected 20 chronic schizophrenics, long stabilized on phenothiazines and long resident in hospital, who had made a good hospital adjustment, who were on full parole, and whom we had not regarded as falling into the category of dejected apathetic inertia. Thus we had not considered them as possibles for anti-parkinsonian drugs.

We ran a double-blind cross-over trial, one month each way, giving in addition to the regular phenothiazine 50 mg. Disipal t.d.s. or its neutral facsimile, and categorized each patient for activity and initiative. In crude terms, for the sake of brevity, our results were: On placebo, 1 much improved, 1 moderately, 0 slightly, 15 not, 3 worse; on active tablet, 4 much improved, 4 moderately, 4 slightly, 8 not improved, 0 worse. This gave χ^2 10.96 and $P < .001$.

The implication of this is that anti-parkinsonian drugs benefit phenothiazine-treated patients who are not manifestly on the threshold of any extra-pyramidal syndrome. There are 3 possible explanations of this.

1. The abolition of the psychomotor retardation of sub-clinical parkinsonism. This has already been discussed and we believe it to be valid.
2. The exerting of an independent psychotropic action. Freyhan (1958) states "Some of these compounds, notably Disipal, are mild stimulants, or exert a psychotropic action of their own". Our own, admittedly limited experience of Artane and Disipal, each used on its own, is that neither has a detectable action as a psychotropic agent.
3. The potentiation of a psychotropic agent. This we feel is likely and applies in addition of course to the first possibility. It may be that the phenothiazines, in their depression of the reticular formation, and consequently their depression of cerebral systems dependent on it, simultaneously depress mood and activity: thus anti-parkinsonian agents do not potentiate psychotropic activity, but rather do they limit the inhibiting action of the phenothiazine.

Our conclusion is therefore that a large proportion of schizophrenics on phenothiazine therapy gain additional benefit from the concurrent administration of Artane and Disipal.

In this we do not mean to exclude other such agents; it is merely due to the fact that so far we have only had time to evaluate these two. Between them we cannot as yet differentiate. We have used Artane the more often simply because it is the one longer known to us. It may well be that Disipal is the superior or that some as yet untried drug is better than either. We shall feel that we have

achieved something if we have indicated a direction in which further research can be profitably directed.

It is a fault of authors of short papers and even sometimes of long ones, not to practise what they preach. To test this last week we counted up the schizophrenics and paraphrenics on the male division who are not involved in any clinical trial. Of 174 such patients, 29 are on Disipal and 60 on Artane; that is to say 89 of 174 or 51 per cent. are on anti-parkinsonian agents, and even more will be when we get around to it.

THE INADEQUATE PSYCHOPATH AT CAMP HILL PRISON

By

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ATTENTION is perhaps insufficiently focused in psychiatry on the "constitutional psychic inferior". It may therefore be of interest to describe prisoners who have been thus affected at Camp Hill Prison in the Isle of Wight.

For many years some of the most afflicted of these people have been a large and important problem in the prison service and a good deal of thought has been applied to their care and management.

Camp Hill Prison contains over three hundred men whose common characteristic is a constitutional inability to deal competently and unaided with the problems of life. Most of them have shown a weakness of personality from an early age. Many give histories of screaming fits, of severe nightmares, of bed wetting, of truancy from home or school, of visits to psychiatrists as children, of quarrels with parents or other members of the family. Many have been inmates of Approved Schools and of Borstal Institutions. Their total disregard for the needs or conveniences of others, their lack of foresight, their tendency to satisfy immediate needs at the expense of future good are marked features in their lives and have led them into much social trouble. Their records with the armed forces are usually poor and in many cases their matrimonial affairs are chaotic.

Camp Hill is a prison set aside for the purpose of Corrective Training (Criminal Justice Act, 1948). It is restricted to persons of not less than twenty-one years of age at the time of conviction. The duration of the sentence is of not less than two years or of more than four years as the Court may determine, and the prisoner must have been convicted on indictment of an offence punishable with at least two years imprisonment. Further he must have been convicted previously since the age of seventeen at least twice on indictment of such or of a similar offence.

On sentence the prisoner is sent first of all to a local prison and thence to an Allocation Centre. There the causes of his antisocial behaviour are studied in relation to his history, mental and physical constitution, personality and temperament by a selected staff which includes psychologists.

There are several prisons for corrective trainees and Camp Hill takes those who appear to need the special conditions of discipline and the closer control and supervision of a maximum security prison.

As is general in prison the corrective trainee can earn by good behaviour the remission of one-third of his sentence, but he must serve the remitted period on licence. Should he not observe the conditions of his licence he is liable to be detained in a "Recall Centre" until the expiration of his sentence.

Over one hundred and fifty prisoners are received each year and each man has a cell to himself. Prisoners are not segregated into different "Halls" according to their individual capacities and peculiarities, but all are mixed

together. The discipline in each Hall is the same and none are more or less restricted than the others.

A few prisoners elect to stay in their cells in the evenings, but most prefer to join in association with their fellows during their leisure hours. This sets a problem for the administration, for weak and inadequate persons when grouped together in large numbers are easily led and tend to follow those who are aggressive and ill disposed. The weak are easily frightened by threats and it is therefore the policy of the authorities to contain the aggressive person sufficiently to permit him to be properly trained in a reasonably free and permissive atmosphere while at the same time protecting the weaker prisoners from their aggressive neighbours. The Governor may on occasion be authorized by the Visiting Committee of the prison or by a Commissioner or Assistant Commissioner to remove a troublesome prisoner for a period of weeks from association with the others. This is an effective measure in most cases (Statutory rule 36).

Timid and fearful prisoners may be given special protection. Efforts are made however to persuade prisoners to stand on their own feet in relation to their fellows, and it is the intention to train them in such a way as to enable them to make correct and sensible decisions. Borrowing tobacco today is unfortunately more important to most men at Camp Hill than repayment of the debt tomorrow. It is often difficult indeed to make them change this life-long attitude.

The average inadequate person has been persuaded by the popular prevailing attitude that his troubles are inherent in himself and are therefore unchangeable by any effort on his own part. That this conception is not entirely true is a proposition that is inculcated here and it is the aim to lessen official support by degrees as a man approaches his release. Supervised work is followed by unsupervised as far as possible. Unfortunately a large proportion of the prisoners are unable to reach such a goal. Standards of work and behaviour are clearly defined and enforced. Most of the men want no more than to get through the sentence with the minimum of effort and it requires much patient and continuous effort to encourage a change in this attitude.

All prisoners who are not ill or restricted by the Medical Officer for medical reasons have to work. Employment is rewarded by small payments and is regulated by a board presided over by the Deputy Governor and attended by those officers most concerned. Most of the prisoners are unable to hold work for any length of time in the outside world and it is probably the chief cause of their presence in prison. Much emphasis is placed upon the correction of this failing.

For those few who are able to reach such a standard vocational training courses are provided in blacksmithing, bricklaying, painting and tinsmithing. In one year six men obtained first-class passes in the City and Guilds examinations. Thirty obtained second-class passes. It will be seen by these small numbers that the general ability of Camp Hill prisoners is not high.

Most men work at simple manual tasks. There are shops for mail bag and filing tag manufacture and employment is found in the kitchen and in the gardens. The big farm employs a good many prisoners and gives training in this work. A few assist the plumbers and electricians as their "mates".

Besides work education plays an important part. Many of the men are poorly educated. There is an illiterates' class which is largely attended. Lessons are also provided in such subjects as English, motor mechanics, leatherwork, pottery, music, first-aid, woodwork, rug making, paper flower manufacture

mathematics and brickwork. Lectures are also given in current affairs, and amateur dramatics and films play their parts. The whole programme is arranged by an Educational Training Officer whose time is shared by Camp Hill and Parkhurst Prisons. His appointment is arranged between the Prison Commission and the Local Education Authorities, and he is responsible for the provision of local teachers and the general supervision of classes. These activities take place in the evening and are voluntary.

The men are young and active and games are therefore provided. They are regarded as the highlight of each weekend. Cricket, football, rugger, table tennis, physical training, gymnastics, weight lifting, basket ball and soft ball are played, and competitions of various sorts arranged.

The Prison is situated in the Isle of Wight from which it is difficult to escape. Its surroundings are fine indeed. It is built on the crest of a hill some two hundred feet above sea level overlooking a distant view of the estuary of the river Medina. Behind is the forest of Parkhurst and the Prison farm of one hundred and ninety acres. It was built in 1912 and it is a full security prison. Its wall encloses six "houses" in each of which are located fifty-five prisoners. In addition there are administrative buildings, workshops and a good kitchen garden.

The whole prison has a cheerful well-kept and modern appearance which is most helpful in training. Each "house" is on two landings and the cells and halls are well lighted and ventilated. The prison hospital is within the wall and so are the chapels for the various religious denominations. The hospital has an open ward and six side rooms with a dental surgery and a small minor operating theatre. The chapels closely resemble outside churches in structure and decoration. There is a good gymnasium which provides space for exercises, for the cinema and for stage productions. The kitchen, bakehouse, baths and lavatories are much the same as those in other prisons. Hot water is supplied to all the houses which are well heated thereby. The shops are large and well constructed and supplied with such machinery as is required for the work in hand.

The Governor is in charge of the prison and he is assisted in this work by three Assistant Governors, a Chaplain, part-time Chaplains of various denominations, a Medical Officer and eighty Prison Officers. Many of these officers are specially trained in various fields of prison employment, and they bring their skill to bear through the trades taught at Camp Hill. From the Governor downwards the staff is on the whole a young one and it is able to bring vigour, strength and a fresh keenness to a difficult task.

Camp Hill and Parkhurst prisons which lie close together are served by three full-time Medical Officers, one of whom gives a high proportion of his time to the work at Camp Hill. His work is medical, surgical and psychiatric. He sees the sick each morning. These average twenty-two daily, which may seem a large number in a young and presumably physically fit population. There is however an hysterical and hypochondriacal tendency in inadequate persons which requires a good deal of attention. Men in captivity often concern themselves with health matters in a way which is less common in free people. They tend to convert their daily troubles into physical symptoms.

Individual psychiatric assessments are regularly made and group interviews are practised. Those who are seriously ill are treated either in the large hospital in Parkhurst Prison or are sent to outside hospitals or clinics. Yearly over fifty prisoners are transferred to the Parkhurst hospital and over one hundred are admitted to the Camp Hill hospital. Forty major operations are performed

on Camp Hill prisoners. Also eighty or more consultations take place with local consultant surgeons or physicians and prisoners attend outside hospitals and clinics about one hundred and fifty times during the same period. The dental work is done by two visiting dentists. Over eleven hundred treatments are given by them. An optician attends the prison and he saw ninety men last year. It is the policy of the Authorities to ensure that as far as is practicable no prisoner leaves at the end of his sentence with disabilities which can be put right if he is willing to have treatment.

As so often happens in psychiatry the diagnosis is not clear cut. Just as the schizophrenic can also have manic-depressive trends or the defective person can be an epileptic so can the inadequate patient suffer from similar complications. One-quarter of all receptions into Camp Hill are much retarded intellectually although they could not be certified as mental defectives under the Mental Deficiency Acts. Only one in eight prisoners received into this prison has a good average intelligence. One in fifty prisoners are epileptic, and one in twenty-five are markedly schizoid. Many have noticeable depressive phases, and there are quite a number who are, for long periods, in an excitable hypomanic state.

An important and possibly underdeveloped aspect of the management of the inadequate is the after care arrangements when he leaves prison. During his training each man is seen by a worker of the Central After Care Association. One interview takes place early in the sentence and another three months before release. After the latter an "associate" is arranged to care for him in the district to which he is being discharged. This associate becomes responsible to the Central After Care Association for the prisoner's proper supervision and he reports to the Central Office of this organization on his progress. Help is given with railway tickets, tools, lodgings, working clothes and perhaps a little money. There is a close liaison between this body and the Unemployment Bureau or the Disablement Resettlement Officer.

When the full sentence has expired the associate's duties end and it is then that the discharged prisoner finds his poor personality is such a handicap. He often has no one to whom he can turn and he falls once more into crime. During the first year following discharge from Camp Hill Prison only twenty per cent are reconvicted. During the second year however when the associate's support has been removed the numbers rise to sixty per cent of prisoners reconvicted. About six months before release a large number of selected men are permitted to go on home leave for a week. The purpose is to acclimatize each of them to the outside world, and each may be thus enabled to arrange future conditions of home and work.

As a national problem that of grossly inadequate people is a small one, but to the family which is unfortunate enough to possess such a person it is a disaster of the first magnitude and it is still one which is largely left to the family or the Prison Service to manage. Perhaps the future will produce a better answer.

The opinions expressed in this paper do not necessarily represent official views but are those of the author himself.

GALVANIC SKIN RESPONSE STUDIES OF SEX RESPONSIVENESS IN SEX OFFENDERS AND OTHERS

By

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INTRODUCTION

THE assessment of sex responsiveness is a recurring problem in the field of conduct disorders and psychopathy, particularly when it is desirable to determine the effectiveness of therapy on the behaviour of the sex offender. Previous studies have indicated certain test differences in emotional disturbance and stress reactivity in subjects of known delinquent history, but it has been observed that sex responsiveness may be an additional (separate) factor to consider for the patient who is a known sex offender (19, 20, 21, 22).

In previous studies we have regarded a recidivistic delinquent act as a conditioned response to stress or anxiety as a learnable drive. If the misbehaviour is sexual in nature, the theory may require that, not only must the stress drive have attained an optimal level, but also sex responsiveness at an optimal level, and that requisite cues were available to elicit the behaviour pattern. One forms the impression that "sex drive"—in popular terminology—is of slight importance in many cases, but responsiveness to cues as a precursor of sexual behaviour is the important aspect to consider, and further, it may possibly be the stress drive level which tends to determine responsiveness to cues, rather than the "sex drive" level.

The first requirement both for therapeutic assessment purposes, and satisfactory research into these points, is the establishment of a technique to indicate the degree of responsiveness to sexual cues. The following notes are concerned mainly with this problem, although the relationship of sex responsiveness to stress tolerance is briefly considered. At this stage, stress tolerance level and sexual responsiveness are regarded as separate factors in the structure of the sex offender.

The simplest suitable index of an "emotional response" is the galvanic skin response (GSR), and similarly, the simplest stimuli providing sufficient ambiguity to overcome the specificity of cues, are words. These two features are taken as the starting point in the search for a satisfactory technique, and current report describes the results of progressive small-scale studies.

THE SUBJECTS

The subjects are (or were at the time of testing), 140 male patients at a State Hospital for mental defectives of "dangerous or violent propensities". They are classified for the purpose of this report as (a) homosexual—those with histories of homosexual misbehaviour, irrespective of other forms of misbehaviour recorded for them, (b) sexual—misbehaviour directed against females or animals, but not homosexual, irrespective of other misbehaviour, (c) violent—misbehaviour that is not homosexual or sexual but includes

violence of a rather severe nature, and (d) miscellaneous—patients who have repeatedly absconded from Institutions, Prisons, etc. and/or have committed misbehaviour not covered by the previous headings, e.g. arson, larceny. All co-operated freely in the research study.

TESTS

1. Intellectual attainment and potential were assessed by the Vocabulary score of the Wechsler Adult Scale, and the Raven's Matrices test, respectively and all were given the Rorschach test.

2. The Leg Persistence Test was used as a measure of pain or fatigue resistance with the score being the sum of the persistence times for the right and left legs taken separately (6, 7, 4, 9, 20).

3. A record of galvanic skin responses was obtained by means of a Theratronics Ltd. G.S.R. recorder, recording by means of a galvanometer needle which carries a high voltage and sparks to an earthed recording plate via teledeltos (sensitive) paper. Palmar electrodes were used dry (i.e. neither electrode paste nor jelly), and gave resistance variations on the record to just beyond one megohm.

4. Three word lists to be known as Word Association Test/1, WAT/2 and WAT/3, were applied on different occasions. The results of WAT/1 are not included in the current study, but this test led to the development of the two later lists. WAT/3 is similar to WAT/2 except for the addition of 2 Homosex words and 2 Neutral words. WAT/3 is given in Appendix I, and it will be seen that the list consists of 3 Sex and/or Homosex words, 2 Sex words, 2 Homosex words, 5 Sadistic/Aggressive words, 5 Arson words, 1 Miscellaneous word and 20 Neutral words. The Neutral words were earlier determined to be low response producers on the GSR records of 50 patients. All the Sex (including Sex/Homosex words) were found to be response producing for patients of I.Q. 55 and above. It will be seen that in the order of presentation (Appendix I) each "emotional" word is followed by a Neutral word and that the entire list is preceded by 5 Neutral words. The words were read out at 15-second intervals and the patient required to give a single verbal association response, whilst the GSR record was being taken.

5. Stress or startle stimulation was obtained by leaving the electrode attached, with instructions to the patient to remain relaxed with eyes closed. When the GSR record stabilized a mild startle was administered by brushing an eyelid with a piece of cotton wool.

6. Following the WAT and "fear" stimuli, the patient was informed that five words would be repeated (as a series), three times, and at the end of each repeated series the eyelid would again be brushed with cotton wool. The word series consisted of Table, Sex, Jacket, Strangle, Floor, and the patient remained with the eyes closed during these repetitions. The repetition provides an index of Incubation and Habituation for the word Sex, and for the "fear" stimulus.

INDICES

The value, and validity, of GSR work is affected to a large extent by the unit of measurement applied (25). Various indices are available, e.g. direct change in resistance, change in conductance (the reciprocal of resistance change), percentage changes, logarithmic scores, etc., but the unit chosen must depend largely upon the objectives of the study and the statistical methods

to be applied to the data (10, 15, 1, 23). There are, however, three main requirements, (a) the unit applied must be independent of basal resistance level, (b) it should allow for manipulation of a zero score, and (c) the apparatus should provide a graphic record. Apart from the practical advantages of graphic recording, there is some evidence that the types of record may be of significance. Records can be classified into Labile, Mixed and Stable (16), and a similar classification is used for the current study, with the addition of a fourth group, Very Stable. For all subsequent calculations in this paper the scores used are relative scores in arbitrary Deflexion Units.

1. *Stress Index*

Paintal (17), reported an index which is obtained by eliciting a "maximum" GSR by means of a faradic shock and relating other deflexions to this unit, and Elliott and Singer (5), found that Paintal's index is unrelated to basal resistance. A similar index has been used in order to investigate persistence variations in disordered mental defectives (20) and found to be correlated with Leg Persistence score to the extent of -0.6 , i.e. high fear score corresponding with low persistence score.

For the current study an index GSRF (for stress or fear) is applied and consists of the relationship of the deflexion produced by the first eyelid touch (MGSR), to the mean score (in Deflexion Units), for the last five Neutral words of the WAT, (NGSR), as follows:

$$\text{GSRF} = \frac{\text{MGSR}}{\text{NGSR}} \times 100$$

Inspection indicates that GSRF differentiates the extremes of the Leg Persistence range, but elsewhere in the range it is less reliable. For 63 subjects a 2×2 chi-squared assessment for the persistence score and GSRF (as dichotomous variables) resulted in a value for chi squared of 6.3, which approaches the 0.01 level of P.

2. *Relative Word Scores*

With the words of the WAT classified as Neutral (N), Sex (S), Homosex (HS), Sadistic Aggressive (SA) and Arson (A), relative scores are available for each of the latter four groups, e.g.:

$$\text{GSR(S)} = \frac{\text{Mean GSR for N}}{\text{Mean GSR for S}} \times 100 \dots \text{for the Sex words.}$$

Similar indices are obtained for GSR(HS), GSR(SA), and GSR(A).

3. *Relative MGSR/Word Score*

The relationship of MGSR—eyelid touch—to the mean score for the words of each type is:

$$\text{M/S.GSR} = \frac{\text{MGSR}}{\text{Mean GSR for S}} \times 100 \dots \text{for the Sex words.}$$

Similar indices are obtained for Homosex, Sadistic Aggressive and Arson words, M/HS.GSR, M/SA.GSR, and M/A.GSR, respectively.

4. Incubation

Bindra and Cameron (2), have reported the results of various GSR experiments into the incubation effect for fear, using a faradic shock. For the current study incubation indices were required—one for the sex stimulus and one for the fear stimulus—in order to investigate relative variations. The index for sex incubation is the relation of the size of the deflexion for the first occurrence of the word Sex, to the size on the second occurrence of the same word in the first repetition series, i.e. second deflexion, and similarly, for fear incubation.

$$\frac{\text{first deflexion}}{\text{first deflexion}}$$

5. Habituation

The indices of habituation for the word Sex and the fear stimulus are determined by dividing the size of the deflexion given on the fourth occurrence of the stimulus by the size of the deflexion occasioned by the stimulus on its first occurrence.

As each of the above indices is a relative score, basal resistance is not taken into consideration. The main advantage lies in the speed of computation, but it is clear that large sudden or gradual changes in resistance invalidate the score, and such records cannot be included in a comparative investigation. All such records (about 5 per cent. of those taken), were rejected in so far as the current paper is concerned.

INVESTIGATION I. COMPARATIVE SEX REACTIVITY (GSR)

1. Primary Response to the Sex Words

The means and standard deviations for groups of unselected subjects in respect of GSR(S) are given in Table I. It will be seen that the Sexual and Homosexual groups give much lower scores than either of the other two groups (low score corresponding with high reactivity), and analysis of variance for the data results in a value for F of 20.17, which is highly significant.

TABLE I

Showing the Mean Scores and Standard Deviations of GSR(S) for the Different Groups of Patients

						N	Mean	S.D.
Sexual ..	..	..	..	..	..	31	38.3	32.6
Homosexual ..	..	..	..	..	..	13	48.9	42.6
Violent ..	..	..	..	..	..	24	70.34	35.9
Miscellaneous ..	..	..	..	..	..	23	58.9	34.0

INVESTIGATION II. INCUBATION AND HABITUATION

1. Introduction

It is suggested that there are three possible explanations for the change in skin resistance during the Word Association Test, any one of which might be the operative factor for a specified patient. The explanations are: (a) the stimuli act as definite cues for the arousal of physiological sex drive, (b) the usage of unexpected "forbidden" words creates a startle response, and (c) the stimuli arouse anxiety associated with the subject matter.

At this stage the possibility that explanation (c)—anxiety arousal—may fire off sex reactivity, or provoke an overt stress CR of any sort, is ignored. Consequently, explanation (a) is fundamentally different from (b) or (c), and

a particular difference is the effect of continued stimulation. Within limits, repetition of a stimulus associated with a primary drive should intensify the physiological correlates of the drive, whereas repetition of a stimulus associated with a stimulus producing response such as fear, without reinforcement, should bring about a decline in the size of the response. Bassett and Ross Ashby report rapid habituation for stimuli similar to the eyeblink startle stimulus used for the current study. Bindra and Cameron (2) however, report the existence of a GSR incubation effect for faradic shock repeated after varying incubation periods. It is observed that an incubation period will produce a larger deflexion for the second occasion of the stimulus than for the first.

In view of these considerations, it appeared possible that the effect, or relative effect, of incubation and habituation on the sex word stimuli, would provide information of psychological significance for the individual patient, and perhaps determine the relative significance of primary GSR deflexions.

2. Incubation Effect

In a study involving 22 Sex (and Homosex) patients and 24 patients without histories of sex misbehaviour (Non-sex), the incubation effect for the fear or startle stimulus was found to be present in 7 and 8 subjects of each group, respectively, with the mean incubation scores for all subjects being 0.75 and 0.76 respectively. Similarly, incubation for the sex word in the repeated series was present in 7 subjects of each group. For the sex word, however, the mean incubation is 0.68 for the Sex offenders, and 1.1 for the others, suggesting a somewhat higher sex anxiety in the Non-sex patients. The ratio between the two incubation scores for these patients provides no suggestive information.

3. Habituation Effect

For the same 22 Sex and 24 Non-sex subjects, more conclusive evidence is provided by Habituation rates. As with incubation, the habituation for fear is roughly the same for the two groups, with mean scores of 0.49 and 0.56 respectively.

Marked intergroup differences are shown for the habituation index for the sex word, and in this case the means are 0.87 and 0.34; 5 subjects from the Sex group showed progressive increases in the size of the deflexion, whereas this phenomenon was shown by only 1 of the other group. Conversely, habituation was complete, i.e. no final deflexion, in only 3 Sex offenders, but in 9 of the other patients. Complete habituation occurred in all cases for the Neutral words.

By regarding the Habituation Index as a dichotomous variable, the following is the contingency table, for which the value for chi squared is 5.74 (P=0.05):

					Sex Habituation Index—HI	
					HI >0.3	HI<0.3
Sex group	..	..	..	..	16	6
Non-sex group	..	..	..	..	9	15

In view of similar intergroup differences being shown by both GSR(S), (the primary response), and the Habituation Index, the possibility arises that the two indices are associated. Two separate rank correlations for 16 subjects of the Sex group, and 13 Miscellaneous patients, respectively, indicate no association between the variables. Owing to tied ranks, tau(b) was the statistic

applied, the respective values being 0.11 and 0.22, neither of which is significant (Kendall, 1948).

The next point to be considered is the relative habituation rate for the fear stimuli and the sex stimuli. If for a given subject the habituation rate for a disturbing stimulus is determined, and that index taken as his habituation norm, the question arises concerning his sex habituation rate relative to this norm. To investigate this, an Habituation Ratio is used, which is the Habituation Index (Sex) divided by the Habituation Index (Fear). If this score is less than unity, sex habituation is more rapid than fear habituation, and the following contingency table for the 22 Sex and 24 Non-sex patients, shows the distribution of the Habituation Ratio, relative to unity; the value for chi squared is 5.46 ($P=0.05$).

						Habituation Ratio (HR)	
						HR >1	HR<1
Sex group	..	..	..	..	..	15	7
Non-sex group	..	..	..	..	..	8	16

4. *Dual Association of Habituation Ratio and GSR(S)*

The independence of HI(S) (Habituation rate), and GSR(S), (primary response), and the fact that each differentiates sex offenders from non-sex offenders at a fairly high level of confidence, but with some overlap in scores, raises the question of the occurrence of low GSR(S) and high Habituation Ratio in the same patient. Such a dual occurrence would indicate initial high responsiveness to sex stimuli, which is equally resistant or more resistant to extinction, than the response to a mild stressor.

By regarding low GSR(S) as score below 45, the following contingency table shows the frequency that this variable occurs together with an Habituation Ratio equal to, or greater than, unity. The subjects are those discussed in the preceding sections.

						Habituation Ratio and GSR(S)	
						HR >1 and GSR(S)<45	HR <1 and/or GSR(S)>44
Sex group	..	..	..	..	..	11	11
Non-sex group	..	..	..	..	..	0	24

The value for chi squared in respect of the above data is 15.41, which is significant at the .001 level. Clearly, the dual occurrence of the two indices in question in 50 per cent. of the sexual offenders and in none of the other subjects, is of particular interest, and can be expected to bear some relation to overt behaviour. It was found from records that the only subjects to have demonstrated sexual misbehaviour whilst under hospital surveillance were those for whom *both* indices were "suggestive". Similarly, the intensity of the earlier misbehaviour was rather more pronounced in those for whom both indices were "suggestive" (using violence as the criterion of intensity), compared with other subjects who had demonstrated more "passive" misbehaviour, e.g. incest; bestiality.

INVESTIGATION III. GSR(S) AND STRESS OR ANXIETY

The original hypothesis, supported somewhat by results discussed above, is that the sex words of the WAT produce greater reactivity in sex offenders, due to the arousal of physiological sex drive and/or stress of sexual content.

Examination of the technique indicates that further features can be expected in the light of the hypothesis. It will be recalled that the sequence of events is first to administer the WAT, and then to elicit the stress response. Hence, if the WAT is high degree stress arousing for *some sex offenders only*, one can expect (a) an association between GSR(S) and GSR(F) for those subjects and not for others, and (b) a consequential independence of GSR(F) and the earlier measured Leg Persistence score, owing to experimental interference with GSR(F) by the introduction of additional stress with the WAT, for sex offenders and not for others. That this is so, is shown by the correlation coefficients given in Table II, where it will be seen that there is no correlation

TABLE II

Showing the Rank Order Correlation Coefficients for GSR(S), GSR(F) and Leg Persistence Scores, each Assessed against each of the Other Indices. N.S. refers to "Not Significant": in Other Cases, the Probability Level is given under "P"

		GSR(S)/L.P.		GSR(S)/GSR(F)		GSR(F)/L.P.	
		Rho	P	Rho	P	Rho	P
Sexual	..	.. -0.15	N.S.	-0.64	.002	-0.24	N.S.
Violent	..	.. -0.23	N.S.	+0.21	N.S.	-0.48	.03
Miscellaneous	..	.. +0.21	N.S.	+0.21	N.S.	-0.4	.07

for Leg Persistence score and GSR(F) for the Sexual group. This is contrary to earlier findings and to the data for the Violent and Miscellaneous groups. Similarly, only the Sexual subjects show GSR(S) scores which are correlated with GSR(F). Both points, therefore, appear to support the hypotheses concerning the stressful nature of the WAT for some Sex offenders, and the consequences of such stress upon other indices.

It is of interest to note that the persistence score which is known to be related to hospital stability, is not indicative of GSR(S) for any group.

INVESTIGATION IV. RORSCHACH COLOUR INDEX

All patients were examined with the Rorschach material prior to GSR testing. Inspection of Rorschach records indicated that the only determinant likely to be of interest was the usage of colour. Significant intergroup differences in respect of Sum C and the frequency of anatomy responses have previously been observed for sex offenders and others in prison (19).

Although there is some confusion concerning the nature of colour responses (11, 12), there is little doubt that the variable is associated with "emotional" or "affective" aspects of personality, although the indices of anxiety may concern only ego involvement anxiety (23). For current purposes it is preferable to restrict statistical examination to two groups: (a) those with Sum C less than unity, and (b) those with Sum C greater than unity (14). Traditional interpretation would *include* anxious, emotionally disturbed, introverted subjects in the former group, and impulsive, emotionally labile, possibly hysterical subjects in the latter.

Thirty-one sex subjects were classified according to the value of Sum C on their Rorschach records, and the values of GSR(S) assessed for each of the two subsequent subgroups. Nineteen patients with Sum C scores less than unity showed a mean score for GSR(S) of 47.15 (S.D. 29.8), and 12 patients with Sum C scores of unity or greater gave a mean score of 27.67 (S.D. 10.28), the variance ratio being 8.1 which is significant at the 0.01 level of P.

In general, those sex offenders giving Rorschach Sum C scores of less than unity demonstrate "passive" misbehaviour such as indecent exposure, or indecent assault on female children, and sometimes show clinical characteristics of hyposexualism. The indication that low Sum C corresponds with *relatively* low GSR reactivity is not, therefore, unexpected.

MISCELLANEOUS OBSERVATIONS

1. *Intelligence and Age*

Random samples of subjects whose GSR scores have been examined above, show Wechsler Vocabulary means as follows: Sex 15.3 (S.D. 4.5; N, 32); Violent 14.8 (S.D. 5.3; N, 24); Miscellaneous 14.0 (S.D. 5.3; N, 23). For the patients in the Sex group there is no indication of an association between GSR(S) and Raven's Matrices score ($\rho = -0.2$).

For the same groups the mean ages are: Sex 28.1 (S.D. 10.03); Violent 26.4 (S.D. 6.8); Miscellaneous 27.9 (S.D. 7.4), and for the Sex group there is no evidence of an association between GSR(S) and age ($\tau(b) = -0.02$). Hence, one can conclude that verbal level, intellectual potential and age have no bearing upon GSR(S).

2. *Type of Record and Psychotic Involvement*

The only observations of relevance to the current study are essentially practical. The Labile and Very Stable records are virtually unscorable, but fortunately form but a small proportion of those taken. A record may appear to be Very Stable owing to polarization of the electrodes, and on the other hand, a fine tremor may create fluctuations on the record suggestive of Lability. Inspection of Mixed and Stable records gives no indication that either are associated with the size of GSR(S).

Psychotic involvement tends to be associated with Lability, particularly when there is gross instability, and GSR(F) tends to be extremely high for epileptics. There is no evidence that mild psychotic involvement invalidates GSR(S).

3. *Homosex Words: GSR(HS)*

The five words forming the Homosex stimuli are Sex, Intercourse, Kiss, Bottle and Bottom. The first three words also form part of the Sex stimuli (hetero) so that there is a necessary association between GSR(S) and GSR(HS). The two words, Bottle and Bottom are such that sexual interpretations are given only by those of homosexual pre-occupation. For other patients these words are *low* response producing, as opposed to lower response producing in the case of the other Sex words. The ambiguity of Bottle and Bottom is apparent from the nature of the verbal responses. This ambiguity (not present for the heterosex words) introduces a new factor into the distribution of scores, which are more scattered.

The means and standard deviations of GSR(HS) for Homosex, Sex, Violent and Abscond patients are given in Table III; analysis of variance for the data results in a value for F of 7.137, which is highly significant. The usage of ambiguous stimuli appears worthy of further study, and the method may carry practical advantages.

TABLE III

Showing Means and Standard Deviations of GSR(HS) for the Four Groups of Disorder Types

	N	Mean	S.D.
Sexual	14	45.2	25.3
Homosex	13	35.2	14.7
Violent	14	92.2	51.9
Miscellaneous	18	69.3	33.4

4. Other Emotional Words

The remaining two groups of stimuli—Sadistic/Aggressive and Arson words—involve personality issues not of relevance to the present paper. However, certain points are of interest. Both groups of words are more clearly indicative of anxiety or fear than is the case for the Sex or Homosex words, and this factor requires close individual interpretation that tends to defy analysis for groups defined according to behaviour disorder; e.g. the word Burn will cause more resistance change in a patient injured in a childhood fire accident than it will for a confirmed arson offender, and sadistic words may be equally stimulatory for the bully and the bullied. The word Child, at present classified as Miscellaneous, has been found to be suggestive of sex pre-occupation for many patients; responses such as "birth", "make", "womb", etc., accompanied by resistance variations are particularly helpful in the interpretation of a specific GSR record.

CONCLUSIONS AND DISCUSSION

From the technological viewpoint one can conclude that the GSR/WAT technique offers a useful method of determining sex responsiveness in offenders, and that habituation indices hold promise of being a necessary adjunct to indices of primary response to word stimuli. The habituation and incubation effects are such that they should be considered in any test-retest comparison of scores. The evidence of the effect of the WAT upon the subsequent eyeblink—fear—response for the Sex group suggests that the interpretation of GSR findings for a disturbed group relative to a control group must take into consideration the possibility that stress (or stimulation) produced in one part of a test may affect scores in a later part. These points would appear to be worthy of direct experimental examination, as the implications extend beyond behaviour disorders and GSR work. In a WAT/GSR investigation of dysmenorrhoea, Boyd and Valentine (1953) similarly observed a "halo effect" for emotional words with resultant higher scores for neutral (as well as emotional) words for the disturbed subjects.

Reaction times for the WAT were examined in a pilot study, but the overlap and interference by extraneous factors such as I.Q. were such to preclude valid interpretation. Variations in the nature of W.A. responses between offenders and normals have been observed by the Psychological Research Wing, India (1953), but the report gives no indication of intergroup differences within the sample. The report draws attention to the high frequency of nil responses given by offenders, and similar observations were made during the current study. Nil responses were found not to inhibit the GSR, however.

Generally speaking, the data indicate that the sex offenders respond more to sexual cues than do other offenders, and within the sex offender group the effectiveness of continued stimulation differs according to the intensity, or nature, of the misbehaviour that has been demonstrated. Hence, one might

conclude that therapeutic interviews of sexual content could vary considerably in the effects on different subjects. Evidence of increased physiological (GSR) activity when sex words are repeated to a patient might be contra-indicative of interview therapy.

Finally, the observations of Garst and Stobin (8) concerning differences in the 17-ketosteroid day to night excretion ratios for non-aggressive sex offenders and controls, and other trends for sex offenders as a whole, appear to be related to the GSR findings of this study.

SUMMARY

The galvanic skin responses of disordered mental defective patients responding to a word association test were assessed in the light of the behaviour disorder shown. The primary response was found to differentiate Sex, Homosex, Violent and Miscellaneous patients at a high level of confidence, and other variations were found for habituation rates, and the habituation ratio of sex stimulus word and a fear stimulus. A dual index was present in 50 per cent. of the sex offenders but in none of the other groups and was somewhat associated with the nature of the sex disorder. Other differences observed include responsiveness to Rorschach colour and primary GSR in the sex group; a varying association of primary sex response with pain resistance (persistence) rating, and variations in responsiveness to Homosex words which indicated possible advantages in the usage of ambiguous stimuli.

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APPENDIX I

<i>Stimulus Word</i>	<i>Classification</i>	<i>Stimulus Word</i>	<i>Classification</i>
(a) Paper	Preparatory	18. Garden	Neutral
(b) Basket	Preparatory	19. FLAMES	ARSON
(c) Shoes	Preparatory	20. Pencil	Neutral
(d) Chair	Preparatory	21. Kiss	SEX AND HOMOSEX
(e) House		22. Newspaper	Neutral
1. Book	Neutral	23. HEAT	ARSON
2. Road	Neutral	24. Clock	Neutral
3. BURN	ARSON	25. BREAST	SEX
4. Table	Neutral	26. Door	Neutral
5. SEX	SEX AND HOMOSEX	27. DEATH	SADISTIC/AGGRESSIVE
6. Jacket	Neutral	28. Picture	Neutral
7. STRANGLE	SADISTIC/AGGRESSIVE	29. DANCE	SEX
8. Floor	Neutral	30. Coat	Neutral
9. INTERCOURSE	SEX AND HOMOSEX	31. BLAZE	ARSON
10. White	Neutral	32. Penny	Neutral
11. FIRE	ARSON	33. HIT	SADISTIC/AGGRESSIVE
12. Ruler	Neutral	34. Pen	Neutral
13. KILL	SADISTIC/AGGRESSIVE	35. CHILD	MISCELLANEOUS
14. Gramophone	Neutral	36. Window	Neutral
15. BOTTLE	HOMOSEX	37. BOTTOM	HOMOSEX
16. Talk	Neutral	38. Hat	Neutral
17. FIGHT	SADISTIC/AGGRESSIVE		

The list of words is in the order of presentation, with 15-second intervals between each word. The various indices are obtained by taking the mean score in deflexion units for the various emotional words relative to the mean score for the Neutral words, e.g. GSR(S)—the mean score for the words 5, 9, 21, 25 and 29, divided by the mean score for the Neutral words: for GSR(HS) the stimuli words are 5, 9, 15, 21 and 37.

AN EVALUATION OF THE PREDICTIVE POWER OF A TEST KNOWN TO DIFFERENTIATE BETWEEN ELDERLY "FUNCTIONAL" AND "ORGANIC" PSYCHIATRIC PATIENTS

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FEW studies of psychological tests which have been shown to differentiate between psychiatric groups have attempted to follow-up the patients originally tested so as to determine what the predictive power of the test might be in the light of subsequent events. One of these few studies has been reported by Walton (1958) and commented upon by Inglis (1959) who was able to show that the test Walton described was better able to predict the outcome of illness after a follow-up period of two years, than was the original diagnostic label. The importance of this kind of study has been pointed out most clearly by Payne (1958). His argument is that, "Description is only one implication of the diagnostic label. Can the test score aid the doctor in making a prognosis? This need not be the case. Let us consider the original validation of the test again. The doctor who diagnosed the standardization group of patients might well be able to give a more or less accurate prognosis for this group of patients. In fact there might be a significant relationship between the presence or absence of the label he assigns, and prognosis. We also know that there is a significant correlation between presence or absence of his label and the *test* scores. *This does not prove, however, that there is any relationship whatsoever between the diagnostic test score and prognosis.* Two things which correlate with the same thing do *not* necessarily correlate with each other, unless the correlations concerned are greater than .7" (1958, p. 27).

The present paper reports the investigation of the predictive power of an adaptation of the Bender Visual Motor Gestalt Test which had already been shown to discriminate significantly between "functional" and "organic" groups of elderly psychiatric patients in a study reported by Shapiro, Post, Lofving and Inglis (1956). The criteria used for the initial diagnostic classification are fully discussed in the latter paper. The differentiation between these groups on the test was achieved through the use of a relatively subjective scoring system which involved a simple rating of each of the patient's drawings.

Shapiro, Field and Post (1957) were able to show that a more objective measure derived from the same test also differentiated the criterion groups at the same high level of significance. This was an angles-measure score which involved the summing, regardless of sign, of the deviations from a right angle of each of the eight angles of two designs. The predictive power of this score is examined in the present study. In each case the angles measure was secured by Dr. Jack Field (1958) in a series of investigations which he carried out on elderly psychiatric patients.

METHOD

Subjects. The individuals followed up had all been patients in the Geriatric Unit of the Bethlem Royal Hospital. Altogether 59 patients were so investigated, although in the numerical data to be reported the overall number is not constant for each variable since some data were not available for all patients. There were 18 men and 41 women, with a mean age of about 69 ($\bar{m}=68.66$; $s.d.=6.23$). Twenty-one of these had originally been diagnosed as "organic" and 38 as "functional".

Follow-up Procedure. The psychiatric social worker tried to follow up each patient individually, as near as possible two years after the patient had been given the psychological test. She succeeded in contacting each patient's relatives and in collecting information under the separate headings given below. This information was then rated by the psychiatrist and by the psychologist, working quite independently, in terms of the criteria and scores listed under each heading, as follows:

A. *The patient's daily routine during his "best" phase of the follow-up period since in-patient stay:*

General Description	Score
Inactive	0
Pottering about and "helping"	1
Employed, doing efficient housework, etc.	2

B. *Evidence for psychological disorders and symptoms, other than cognitive, since period in hospital:*

General Description:	Score
Continuously severely disabling	0
Continuously mildly disabling	1
Intermittently severely disabling	2
Intermittently mildly disabling	3
No psychological disturbance at any time	4

C. *Evidence of cognitive disturbances and intellectual changes since in-patient period:*

General Description:	Score
Definite	0
Dubious	1
None	2

D. *Evidence of personality changes since in-patient period:**General Description:*

Score

Never anything like his old self, or continuously ill	0
Mild invalidism	1
As well as, or "better than" before illness	2

In addition to these items other evidence was gathered by the psychiatrist on several topics. A note was made, for example, of any changes in diagnosis. This item did not, in fact, prove to be of any importance since, after a space of two years, only one patient had been re-diagnosed; this was a patient originally labelled organic who was later re-categorized as functional. Account was also taken of the number of months the patient had spent in any hospital from the date of testing, expressed as a percentage of the follow-up period. Finally it was noted if the patient were still alive or not.

RESULTS

The results obtained may be conveniently considered in terms of three problems.

1. To determine the degree of reliability of the independent ratings made by the psychiatrist and the psychologist of the data gathered by the social worker.

2. To examine the prognostic power of the first diagnosis in terms of its correlation with the various estimates made of the outcome of illness over the two-year period.

3. To examine the predictive power of the test score in the same terms.

1. *The Reliability of the Ratings*

The reliability of the independent ratings made of the social worker's notes by the psychiatrist and the psychologist was simply assessed by running product-moment correlations (McNemar, 1949) between the two sets of ratings. The results are shown in Table I.

TABLE I

Product-moment Correlations Between Ratings Made Independently by the Psychiatrist and the Psychologist

								r
A. Best daily behaviour	..	..	..	..	..	..	..	0.87*
B. Non-cognitive disturbances	..	..	..	..	..	..	..	0.66*
C. Intellectual changes	..	..	..	..	..	..	..	0.85*
D. Personality changes	..	..	..	..	..	..	..	0.90*
Sum of ratings (A+B+C+D)	..	..	..	..	..	..	..	0.92*

* Significant at or beyond the 1 per cent. level.

It can be seen that the correlations obtained reflect a large amount of agreement between the two raters. This shows that the criteria used could be regarded as reliable indicators of the patients' state as described in the social worker's notes.

As most of the patients had been known to the psychiatrist since their first admission to hospital his ratings were accepted as being probably the more valid and these were therefore used in the attempts to elucidate the further problems examined.

2. The Prognostic Power of the First Diagnosis

In order to discover what indications the first diagnostic label might hold for the subsequent developments, as assessed by the various estimates secured, bi-serial correlations (McNemar, 1949) were run between the dichotomous diagnostic variable (i.e. functional or organic) and these estimates are shown in Table II. It should be noted that since the first diagnosis and the alive-dead classifications are both dichotomous a contingency coefficient (McNemar, 1949) was taken as the appropriate measure of association in this instance.

TABLE II
Bi-serial Correlations (etc.) Between First Diagnosis and the Variables Estimated in the Follow-up Study

	r bis.
First diagnosis $\times$ Best daily behaviour	0.59*
First diagnosis $\times$ Non-cognitive disturbances	0.48*
First diagnosis $\times$ Intellectual changes	0.57*
First diagnosis $\times$ Personality changes	0.54*
First diagnosis $\times$ Sum of 4 ratings made by the psychiatrist	0.76*
First diagnosis $\times$ Percentage time in hospital	-0.21 N.S.
	c.c.
First diagnosis $\times$ Alive or dead	0.48*

* Significant at or beyond the 1 per cent. level.

N.S.=Not significant.

Table II shows that the first diagnosis has quite a significant relationship with the effects of the illness over the subsequent 2 years on a variety of estimates.

Patients diagnosed "functional" were, as one would expect, on follow-up significantly better adjusted to life, showing fewer psychiatric symptoms, fewer intellectual and personality changes, and were more often still alive, than those who at the time of testing had been clinically diagnosed as suffering from psychiatric illnesses associated with cerebral pathology. Functional patients had also spent less time in hospitals, though not to a significant extent. This, too, is not surprising for the following reason: though organic mental patients are more likely to become permanent hospital inmates, it has been shown recently (Colwell and Post, 1959) that "functionals" also tend to spend relatively long periods in hospital during the first two years after admission on account of their unfortunate tendency to recur at an early date.

It remains to be seen how the prognostic power of the clinical diagnosis compares with the relation between the same estimates and the test score.

3. The Predictive Power of the Test

(a) *The Group as a Whole.* For all the patients studied, simply considered as one group, the relation between the angles-measure score and most of the other variables could be estimated by product-moment correlations. The only exceptions were the relations between the test score and the dichotomous variables (i.e. first diagnosis, second diagnosis and alive-dead) and in these cases a bi-serial correlation was used. The results for the group as a whole are shown in Table III.

The predominance of negative correlations is simply due to the fact that a high score on the angles measure was characteristic of greater pathology whereas the reverse was true of most of the follow-up variables.

It is only to be expected that there should be significant relations between the test score and first and second diagnosis. This is merely another indication

TABLE III

Product-moment Correlations (etc.) Between the Angles-Measure Score and the Variables Estimated in the Follow-up Study for the Group Considered as a Whole

					r	
Angles measure × Best daily behaviour	..	..	..	..	-0.26	N.S.
Angles measure × Non-cognitive disturbances	..	..	..	..	-0.16	N.S.
Angles measure × Intellectual changes	..	..	..	..	-0.46*	
Angles measure × Personality changes	..	..	..	..	-0.20	N.S.
Angles measure × Sum of 4 ratings made by the psychiatrist	..	..	..	..	-0.28	N.S.
Angles measure × Percentage time in hospital	..	..	..	..	-0.23	N.S.
						r bis.
Angles measure × Alive or dead	..	..	..	..	0.01	N.S.
Angles measure × First diagnosis	..	..	..	..	-0.38†	
Angles measure × Second diagnosis	..	..	..	..	-0.41*	

* Significant at or beyond the 1 per cent. level.

† Significant at or beyond the 2 per cent. level.

N.S. = Not significant.

of the fact that the test successfully discriminated between the criterion groups.

It is, however, disappointing to find that for most of the follow-up variables the test appears to lack any predictive significances whatever. An interesting exception is provided by the significant correlation between the angles measure and follow-up evidence of intellectual decline. Even this, however, is certainly no better than the prognostic significance of the first diagnosis in relation to these same functions. (see Table II)

(b) *The Diagnostic Groups Considered Separately.* It would be possible to argue that even if the test had little predictive power for the group taken as a whole it might be more successful for one diagnostic group than for the other. Product-moment correlations were therefore run between test score and the other variables for the two groups separately. Since the alive-dead dichotomy entered into the calculations a bi-serial correlation was calculated in this case. The results are shown in Table IV.

TABLE IV

Product-moment Correlations (etc.) Between the Angles-Measure Score and the Variables Estimated in the Follow-up Study for the Groups Considered Separately

					Functional r	Organic r
Angles measure × Best daily behaviour	..	..	..	..	0.02 N.S.	-0.05 N.S.
Angles measure × Non-cognitive disturbances	..	..	..	..	-0.03 N.S.	0.13 N.S.
Angles measure × Intellectual changes	..	..	..	..	-0.11 N.S.	-0.29 N.S.
Angles measure × Personality changes	..	..	..	..	0.06 N.S.	0.06 N.S.
Angles measure × Sum of 4 ratings made by the psychiatrist	..	..	..	..	0.11 N.S.	-0.06 N.S.
Angles measure × Percentage time in hospital	..	..	..	..	-0.16 N.S.	-0.10 N.S.
						r bis.
Angles measure × Alive or dead	..	..	..	..	-0.001 N.S.	0.12 N.S.

N.S. = Not significant.

Again it can be seen that there is little or no relationship between the test score and the estimates made of the patient's state during the follow-up period. The test cannot, therefore, be used to predict either a malignant or a relatively benign course of the illness in patients with organic psychoses, nor will it

indicate the amount of future disabilities in the case of functional psychiatric disorders.

DISCUSSION

The results of this investigation confirm most strongly the contention made by Payne (1958) that psychological tests must be directly validated for the purpose to which they are being put. The present investigation has demonstrated that even a test which has been validated and cross-validated in terms of its classificatory power does not necessarily have the predictive or prognostic power of the classificatory system against which it was initially standardized.

It is possible that this failure may be, in part at least, due to the indirect nature of the relation between the functions which are probably measured by the test and the psychiatric disturbances. After all, the inability to copy drawings is not a symptom of which elderly patients commonly complain; nor has it usually been regarded as a cardinal sign of disorder in those patients by the clinician. It may be that a more profitable approach to the discovery of those psychological variables which *do* carry some of the implications of valid psychiatric diagnosis will be made rather in the direct study of the principal descriptive characteristics of psychiatric disturbances. Such a method has, for example, been attempted by Inglis (1957) in the experimental investigation of memory disorder in elderly psychiatric patients.

The present study, on the other hand, successfully reconfirms the usefulness of psychiatric classification of elderly patients in terms of "functional" and "organic" syndromes, and is in line with other recent follow-up studies (Post, 1951; Roth and Morissey, 1952; Norris and Post, 1954).

SUMMARY

This study reports on the investigation of the predictive power of a test known to discriminate between certain psychiatric categories. It was shown that reliable ratings could be made of the content of follow-up notes made by the psychiatric social worker. When, however, the test was assessed against these and other objective criteria it was shown that it did not have the prognostic power demonstrated by the original psychiatric diagnosis.

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DEMENTIA: A CLINICAL AND EEG STUDY OF 274 PATIENTS OVER THE AGE OF 60

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INTRODUCTION

THE purpose of the investigation was the assessment of dementia from a clinical and EEG viewpoint in patients aged 60 and over, resident in a mental hospital containing a high proportion of elderly long-stay persons. All patients of suitable age were examined irrespective of diagnosis, provided that this was technically possible and, if alive, they were re-examined three years later, in the hope that a longitudinal study would give additional information as suggested by Roseman *et al.* (1952) and Sheridan *et al.* (1955).

The clinical assessment of dementia is of necessity somewhat vague and subjective. Because of this, correlation with EEG findings was attempted in two surveys on aged patients in dissimilar hospitals. The first, already reported (Turton, 1958), concerned a unit taking primarily short-term patients of good prognosis. The findings obtained did not lend any support to the view that the EEG was of value in differentiating between mild dementia and depression with agitation or retardation.

In the investigation described herewith, it was hoped that a group in which dementia was prominent in a considerable proportion of cases, might yield further information about the nature and extent of EEG changes in old age. Luce and Rothschild (1951, 1953) felt there was a direct correlation between EEG abnormality and the degree of mental impairment in elderly patients. McAdam and McClatchey (1952) found very few abnormal records in patients over 60, who did not show evidence of clinical deterioration and, later, McAdam and Robinson (1956, 1958) using rating scales showed a trend of conformity between clinical and EEG assessments.

These findings were essentially confirmed by Mundy-Castle *et al.* (1954) and Silverman *et al.* (1955). More recently, Obrist and Henry (1958) found that 88 per cent. of a group of aged psychiatric patients with a functional disorder had normal tracings, whereas 79 per cent. of patients suffering from "brain syndrome" showed diffuse slow waves on the EEG.

However, not all workers have found so satisfactory a correlation between EEG findings and the clinical estimate. Liberson and Seguin (1945) stressed that a third of definitely organic patients have a normal or a borderline normal record. Strauss and Greenstein (1948), examining patients with cerebrovascular disease found that 67 out of 95 had records with no slow activity. Even severe C.N.S. lesions were associated with a normal record in 24 patients.

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Weiner and Schuster (1956) found that only a half of their patients with minimal dementia had abnormal records.

Furthermore any abnormal EEG findings have to be assessed and compared with the known changes that occur in elderly persons (Obrist, 1951; Silverman *et al.*, 1955; Maggs and Turton, 1956). It was for this reason that it was considered desirable to investigate as large a sample as possible.

METHOD

(a) *Physical Examination*

Each patient was examined physically, particular attention being paid to the nervous and cardiovascular systems. Illnesses occurring between the two EEG examinations were noted and any change in physical signs.

(b) *Assessment of Dementia*

Dementia was assessed on clinical grounds, from the patients' general behaviour and performance and simple tests of information and orientation; in addition, each patient was tested for his digit span and his performance with the Babcock Sentence (Zangwill, 1943).

Dementia was graded according to the following scale:

- (i) *Absent*: No evidence of dementia clinically or with tests.
- (ii) *Minimal (+)*: No evidence of dementia clinically. Diminished digit span and/or impaired performance with Babcock Sentence.
- (iii) *Moderate (++)*: Organic dementia would be suspected on clinical grounds. There was definite impairment of recent memory, difficulty in solving simple sums, often some disorientation, and impaired performance on the tests. There was no deterioration in habits or character.
- (iv) *Severe (+++)*: Obvious dementia clinically. In addition to a more severe impairment of memory, information and orientation, impaired digit span and meaningless attempts at the Babcock Sentence, there was some deterioration in habits—viz., unkempt appearance, urinary incontinence, crude feeding and often some disinhibition in behaviour.
- (v) *Gross (++++)*: These patients were mostly in bed and doubly incontinent. There was gross memory impairment and disorientation. Much of their speech was meaningless.
- (vi) *Not Tested*: These patients were all schizophrenics, many of them mute, and it was not possible to grade them according to the above scale because of their lack of co-operation in testing, or because of doubt as to whether deterioration in behaviour derived as much from psychosis as dementia.

In addition to assessing the degree of dementia, an attempt was made to classify the patients with respect to the type of dementia from which they suffered, viz., Presenile, Senile, Arteriosclerotic, G.P.I., and Dementia following head injury, carbon monoxide poisoning, alcoholism and epilepsy of long standing.

Arteriosclerotic dementia was diagnosed on the grounds of the history and associated physical signs, viz., history of minor or major strokes, and abnormal

C.N.S. signs associated with these, arteriosclerotic Parkinsonism, hypertension ($>190/110$) and hypertensive changes in the optic fundi. Cases without these signs and beginning after the age of 65 were classified as senile.

(c) *EEG and Criteria of EEG Abnormality*

The majority of the records were taken on a 6-channel portable machine, although a few were recorded on a conventional Ediswan 8-channel electroencephalograph. The portable machine was used so as not to upset easily agitated senile patients by removing them to strange surroundings. The recording was thus effected in the patient's ward or in close proximity to it. Even so a considerable number of the patients were too disturbed for a satisfactory recording on either the first or second occasion and this inevitably introduced some bias into the sample. Only those records which were of a satisfactory length and comprised a reasonable number of electrode patterns were accepted. The records were all reported by one of us (E.C.T.) according to a fixed pre-arranged plan, and without any clinical information whatsoever about the patient.

Apart from the records classified as normal the following five groups were recognized:

- (i) *Borderline Normal*. These almost all showed a definite excess of fast activity with little or no alpha rhythm and usually some increase in the theta component.
- (ii) *Generalized Slow Wave Changes of Moderate Degree*. These records showed a definite increase in the slower rhythms persistently in all or most areas of the cortex. Focal or localized changes were in some cases present but were not outstanding.
- (iii) *Generalized Slow Wave Changes of Severe Degree*. The changes were similar to those noted above but they were more marked and always consisted of a delta dominant record, usually with waves of low frequency and high amplitude.
- (iv) *Focal Slow Wave Changes*. These records showed predominantly a delta focus although there might be associated diffuse changes as well.
- (v) *Epileptic Changes*. The records showed changes of the kind which would normally be considered of a characteristic epileptic pattern whether localized or generalized.

No patients were included who were on a high dosage of barbiturates or other drugs and, in fact, the majority were on no drugs at all although a few received nocturnal sedation. No patients had been treated with E.C.T. within three months of the recording. The subjects were awake and not hungry.

RESULTS

The total number of cases studied was 274, of whom 110 were male and 164 female. Thirty-one (28.4 per cent.) of the males died and 43 (23.2 per cent.) of the females. The overall death rate for males and females for the three-year period of study was 27.4 per cent. There was no significant difference in the death rate as between the sexes or in the age groups 60-69 and 70-79. The death rate was slightly higher in the 80-89 age group in both sexes, and both patients aged 90+ at the beginning of the study died. Neither the presence of EEG abnormality, nor the type of EEG abnormality if present, had any

relation to the death rate, and the actual causes of death were in the great majority of cases quite unrelated to EEG abnormality.

The death rate did vary, however, according to the clinical diagnosis:

	Number of Cases	Deaths	Death Rate Over 3 Years (Per cent.)
Total	274	74	27.4
Arteriosclerotic dementia	15	5	33
Senile dementia	22	12	54
Senile paranoid psychosis	21	8	38
Schizophrenia	125	24	19
Affective psychosis	59	11	19
Epilepsy	12	6	50

TABLE I

	Number of Cases	Normal EEG	Abnormal EEG
"Normals" (Maggs and Turton, 1956)	82	38 (46%)	44 (54%)
All cases this series	274	133 (48%)	141 (52%)
No dementia	93 (30%)	57 (61%)	36 (39%)
Dementia not tested	77 (28%)	36 (46%)	41 (54%)
Dementia+	16	5 (25%)	11 (75%)
Dementia++	34	20 (60%)	14 (40%)
Dementia+++	32	12 (37%)	20 (63%)
Dementia++++	21	2 (7%)	19 (93%)
All dementia	103	39 (30%)	64 (70%)
All dementia>+	87	34 (39%)	53 (61%)
Presenile dementia	4	2	2
Arteriosclerotic dementia	15	3 (20%)	12 (80%)
Senile dementia	22	3 (14%)	19 (86%)
Schizophrenia	125	70 (56%)	55 (44%)
Affective psychosis	59	32 (54%)	27 (46%)
Senile paranoid psychosis	21	9 (43%)	12 (57%)
G.P.I.	5	4	1
Mental defect	5	4	1
Epilepsy	12	3 (25%)	9 (75%)

The General EEG Picture

The following observations may be made from an examination of Table I.

- (i) The number of abnormal EEGs (52 per cent.) in this series taken as a whole is almost exactly the same as that found by Maggs and Turton (54 per cent.) in their series of normals over the age of 60.
- (ii) If we compare the proportion of EEG abnormality (70 per cent.) in all those showing dementia with those showing no dementia on testing (30 per cent. abnormal EEGs), we find that the likelihood of an abnormal EEG is greater if dementia is present.

($\chi^2=10.73$, which is significant at 0.01 level.)

Even so, we may still observe the number of abnormal EEGs among those graded as having no dementia, and the 39 normal records among

the 103 patients who exhibited dementia in some degree. The Table shows that normal records were still found among those graded as severely or grossly demented.

- (iii) If, however, we compare the incidence of EEG abnormality among those having a definite organic dementia (presenile, senile, arteriosclerotic and G.P.I.) with those having no dementia, then the relationship between dementia and EEG abnormality is a good deal closer.

($\chi^2=15.26$, which is significant at the 0.001 level.)

It may be that the relationship between EEG abnormality and organic dementia would have been a little closer had our clinical estimate of dementia been more accurate—i.e. that in spite of excluding 77 patients as being unsuitable for testing, we may still have graded some deteriorated schizophrenics as being demented when they were not. A comparison of the figures for definite organic dementia with those for all patients classified as demented lends some support to this view.

($\chi^2=4.9$, which is significant at the 0.05 level.)

- (iv) The figures for senile paranoid psychosis and for those in whom it was impossible to test for dementia were substantially the same as for a group of normals.
- (v) The number of cases of presenile dementia is too small for analysis, although 2 of the 4 had normal EEGs; however, we did not do barbiturate and stimulation studies, such as those reported by Letemendia and Pampiglione (1958) or Liddell (1958).
- (vi) The figures for schizophrenia and affective psychosis are similar, and show a slightly higher proportion of normal EEGs than the "normals".

EEG Changes After 3 Years

Although all 200 of the 274 patients who survived the three-year period had repeat physical examination and assessment of dementia, it was only possible to repeat the EEG on 190.

Of these 190, there was no EEG change in 162.

Twelve normal records showed moderate or severe diffuse slow-wave change on the second examination and one borderline record and one showing focal changes, showed moderate diffuse slow activity. One showing moderate slow activity showed a delta dominant record after three years and one normal record revealed epileptic changes. Only 16 of the 190 records, then, changed for the worse.

Twelve records showed improvement after three years (Borderline→normal, 2; Moderate slow→normal, 7; Moderate slow→borderline, 1; Epileptic→borderline or normal, 2).

Changes in Degree of Dementia and Change in EEG

In 9 patients dementia was judged to have increased over the three-year period; in 7 of these, the EEG remained unchanged, and in 2, there was a commensurate change in the EEG.

C.N.S. Signs and the EEG

Abnormal C.N.S. signs were present in 41 patients; 28 of these had abnormal EEGs and 13 were normal in this respect. In 13 patients there were

changes in C.N.S. signs between the two examinations, but only 4 of these showed a change in the EEG.

Further EEG Results

There was very little difference in the EEG pattern between the sexes or between the age-groups 60-69, 70-79, and 80-89.

The most common abnormality was a moderate degree of diffuse slow-wave change, and this was frequently present in patients with no dementia and among those who could not be tested. A severe degree of diffuse slow-wave change does, however, appear to be associated with dementia, although it may be objected that the number of cases showing such changes is small (9 out of 21 cases of gross dementia).

We could not associate any particular type of EEG abnormality with any of the various diagnostic groups. Again, when abnormality was present, a moderate degree of diffuse slow-wave change was the most common. Delta-dominant records and focal abnormalities were found only in those cases of dementia classified as arteriosclerotic or senile.

The number of borderline-normal EEGs was rather fewer than in previous series of this kind. The proportion was slightly higher in females and in the age-group 60-79. The finding had no relation to dementia or to the clinical diagnosis.

DISCUSSION

The results in this investigation are similar to those obtained by one of us (Turton, 1958) investigating predominantly a quite different type of clinical material in a dissimilar hospital. Furthermore, despite the large numbers of persons investigated over a three-year period the actual value of the serial recordings proved to be slight, in contradistinction to the findings of Sheridan *et al.* (1955) who stated that it was exceptional for serial recordings taken at three-monthly intervals on one individual with a chronic brain syndrome of either arteriosclerotic or senile origin to remain unchanged.

Between severe organic deterioration and EEG changes the correlation was good, but until this degree was reached, the EEG was of no value in assessing the degree of mental involvement. This work therefore does not support the value of the EEG as a diagnostic weapon in the assessment of degree of dementia as some authors such as McAdam and Robinson (1956, 1958) have claimed. Furthermore, as a normal record is not infrequently found in a patient with obvious clinical impairment and an organic mental syndrome and an abnormal record in persons with no clinical signs or symptoms, the EEG may be positively misleading. Our results in this respect differ from those of Pampiglione and Post (1958), who concluded that patients over 60 with psychiatric disorders free from obvious clinical signs and symptoms of cerebral organic disease only rarely have abnormal EEGs, that a normal EEG is rare in the presence of definite clinical evidence of organic disease, and that a definitely normal EEG rules out important brain changes. Our results are disappointing, as an objective method of assessing the degree of dementia would be of value not only in "mixed" cases where there is a suspicion of dementia underlying depression but also where, by reason of psychosis, clinical examination is unsatisfactory.

It appears that the electrical response of the human brain varies widely from individual to individual under similar circumstances of stress. Until the

nature of the compensating mechanism is more clearly defined, the reasons for the large individual variations encountered cannot be truly assessed.

SUMMARY AND CONCLUSIONS

1. Two hundred and seventy-four patients between the ages of 60 and 79 were examined over a three-year period. This consisted of physical examination, assessment of dementia and EEG; it was only possible to perform repeat EEG examination on 190 out of the 274 patients, and repeat clinical examination on 200.

2. The criteria for dementia and for EEG abnormality are defined.

3. Although EEG abnormality is more likely in the presence of dementia where dementia is judged definitely to be absent, there are still a considerable number of abnormal EEGs even in the latter group and of normal EEGs where there is no clinical doubt about dementia. This statement holds good even in groups diagnosed as suffering from senile, arteriosclerotic and presenile dementia, and G.P.I., although EEG abnormality is more likely in these cases.

4. There is little correlation between clinical estimate of the degree of dementia and EEG abnormality, except where dementia is gross and obvious.

5. The results indicate that the EEG is of little help to the clinician when he cannot assess underlying dementia because of co-existent psychosis.

6. The proportion of EEG abnormality in patients suffering from schizophrenia, senile paranoid psychosis and affective psychosis was similar to that of a group of normals of the same age.

7. There was no correlation between change in degree of dementia and EEG change, but abnormalities on clinical examination of the C.N.S. were usually reflected in the EEG.

8. There was no EEG abnormality which could be said to be characteristic of any particular type of dementia in this series. The most common abnormality was a moderate excess of diffuse slow activity.

9. Of the 190 EEGs which were repeated after three years, 162 showed no significant change, 15 showed an increase in the amount of slow activity present and 12 returned to normal.

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TISSUE LEVELS OF CHLORPROMAZINE IN EXPERIMENTAL ANIMALS*

By

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THE increasing use of tranquillizers in the treatment of mental disorders has made it imperative to study both the immediate and long-term effects of these drugs in order to establish their limits of safety. One of the approaches that appeared important to us was the correlation of the histological findings (Roizin, True and Knight, 1959) with tissue levels of the drug. In addition to its significance from the pathological standpoint, such a study may also furnish information towards a better understanding of the mechanism of action of these drugs.

A few reports have appeared in the literature on the distribution of chlorpromazine in the tissues of animals' organs and different brain areas (Salzman and Brodie, 1956; Fedorov and Schnol, 1956; Fedorov, 1957; Wase, Christensen and Polley, 1956). Except in one of these studies (Salzman and Brodie, 1956) S_{35} labelled chlorpromazine was used.

This paper describes results of a systematic investigation in which chlorpromazine levels were determined in the tissues of rats and monkeys following single acute or repeated chronic dosages of the drug.

EXPERIMENTAL

I. Acute Experiments

(a) *Rats*: Chlorpromazine hydrochloride (SKF Thorazine)† was injected intramuscularly into white Sprague Dawley rats at a level of 10 and 25 mg. per 100 g. body weight respectively. The average weight of the rats was 300 g. The animals were sacrificed 16 to 18 hours after injection and drug determinations carried out on the tissues according to a recently-published method (Wechsler and Forrest, 1959). Briefly it consists of extracting the chlorpromazine from tissue, oxidizing it to the sulphoxide level and measuring it as such in the ultraviolet range of the Beckman DU spectrophotometer. Chlorpromazine sulphoxide has maxima at 300 and 340 $m\mu$. In each case the concentration was calculated at both the wavelengths and mean values taken. Control tissue from

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† We gratefully acknowledge the generous supply of chlorpromazine from Smith, Kline & French Laboratories.

untreated animals was subjected to the same procedure. The optical density values for each organ (several experiments) were averaged and subtracted from the readings obtained with the tissues of chlorpromazine treated animals.

(b) *Monkeys*: The procedure was similar to that with rats except that 15 mg. chlorpromazine per 100 g. body weight was injected subcutaneously instead of 25 mg. and the animals sacrificed 16 to 18 hours after injection. It was felt that exceeding the 15 mg. per 100 g. body weight dosage would greatly increase the danger of the drug being fatal, a consideration more important in the case of costly monkeys than rats.

II. Chronic Experiments

Rats were injected daily with 0.6 mg. chlorpromazine per 100 g. body weight for periods from two weeks to three months. Drug determinations were carried out on the same tissues as in the case of acute experiments.

Brain and liver samples from two monkeys sacrificed after daily injections of chlorpromazine for 20 and 30 months respectively were also analysed for the drug.

In all of the above experiments, acute and chronic, the tissues were either used when fresh or else after storage in the frozen state since it was found that with the exception of the stomach and intestine, freezing did not influence the chlorpromazine level. However, freeze storing the above two organs often resulted in a partial or complete loss of the typical UV chlorpromazine sulphoxide absorption peaks and thus indicated structural changes. This may have been due to the effect on chlorpromazine of the respectively acid and alkaline pH of these two organs.

RESULTS

I. Acute Experiments

The values in Table I represent averages of several acute experiments.

TABLE I
Chlorpromazine Content in Rat Tissues

	Dose of Cpz.*	25 mg./100 g.b.w.		10 mg./100 g.b.w.	
		(µg./gm. Tissue)			
Liver		501		161	
Brain		91		trace	
Lung		713		475	
Spleen		349		123	
Kidney		207		101	
Intestine		179		167	
Stomach		238			
Heart		72		0	
Skeletal muscle		103		trace	
Spinal cord		trace		0	
Uterus		69			
Ovaries		150			
Adrenals		386			

* Cpz=Chlorpromazine.

However, because of the size of some of the organs (adrenals, ovaries, etc.) samples had to be pooled from several rats in order to obtain sufficient measurable tissue and fewer experiments could therefore be carried out in these instances.

When 25 mg. chlorpromazine per 100 g. b.w. was injected in rats the largest amount of the drug was found in the lungs. This was followed by liver, spleen, stomach, kidney, intestine, etc. The brain contained less than any of these organs.

The adrenals of 17 rats totalling .7 g. contained a rather large amount of chlorpromazine, i.e. 386 μ /g. tissue. The experiment could not be repeated on the same scale and determinations on adrenals from individual rats showed only traces of the drug, not an unexpected finding in view of the minute amount of tissue.

Experiments in which 10 mg. chlorpromazine per 100 g. b.w. was injected also showed that the lungs had the largest amount of the drug, followed by the intestine, liver, spleen and kidney (Table I). Except for the intestine the values were roughly from one-half to one-third of those with the 25 mg. per 100 g. b.w. dosage.

The distribution of chlorpromazine in different parts of the nervous system of monkeys injected with the 15 mg./100 g. b.w. is shown in Table II.

TABLE II
Chlorpromazine Content in C.N.S. of Monkeys

	μ g./gm. tissue								
Frontal lobe	..	..	..	..	..	..	..	..	52
Occipital lobe	..	..	..	..	..	..	..	..	50
Brain cortex	..	..	..	..	..	..	..	..	46
Basal ganglia	..	..	..	..	..	..	..	..	60
Spinal cord	..	..	..	..	..	..	..	..	21
Cerebellum, pons	..	..	..	..	..	..	..	..	trace

As can be seen there is not much difference in the drug level between the basal ganglia and cortex, but the spinal cord and cerebellum is lower with only a trace found in the latter (in two of the three determinations). The same was true for the pons.

Of the examined organs (Table III), the lungs had the largest amount of

TABLE III
Chlorpromazine Content in Monkey Tissues

	μ g./gm. tissue								
Lung	..	..	..	..	..	..	..	..	234
Spleen	..	..	..	..	..	..	..	..	105
Liver	..	..	..	..	..	..	..	..	98
Adrenals	..	..	..	..	..	..	..	..	81
Kidney	..	..	..	..	..	..	..	..	64
Ovary	..	..	..	..	..	..	..	..	56
Heart	..	..	..	..	..	..	..	..	trace

chlorpromazine as was the case with the rats, followed by spleen and liver. The adrenals (weighing 0.9 g. and 0.5 g. per pair respectively) contained almost as much chlorpromazine as the liver thus paralleling the high levels obtained with the pooled rat adrenals (Table I).

II. Chronic Experiments

No chlorpromazine was found in any of the examined rat tissues and in liver and brain samples of monkeys. The amount injected (see experimental section) corresponded to therapeutic doses in humans. Thus within the limits

of the method, no chlorpromazine accumulation could be demonstrated in organs of rats receiving repeated low dosages of the drug and by analogy this suggests the possibility that a similar lack of accumulation exists in patients treated with the usual dosages of the tranquillizer.

DISCUSSION

Although experimental conditions were different some comparison can be made between our findings and those of other workers. We have previously pointed out the difficulties connected with the determination of chlorpromazine in biological material (Wechsler and Forrest, 1959) and the belief that our tissue method eliminated most of them. Inadequacies of the Salzman and Brodie method (1956) as judged from the poor recoveries especially with tissues of some of the organs as well as differences in species and experimental conditions may account for the different drug distribution in the organs of dogs which these workers have reported. On the other hand, there is good agreement between our results and those of Fedorov (1957) and Fedorov and Schnol (1956) who like us have also found (using rats, dogs, and rabbits as experimental animals) the highest amount of chlorpromazine in the lungs followed by the liver with much lower levels in the brain cortex. The Russian workers did not find any significant differences in drug accumulations in different brain areas which is in contrast to the findings of Wase, Christensen and Polley (1956) who reported much higher levels of chlorpromazine (at least the first day after injection) in the hypothalamus, thalamus, pons and cerebellum than in the cortex. Both groups of investigators used S_{35} labelled chlorpromazine. Although the hypothalamus was not included in our studies of the C.N.S., our results seem to be more in agreement with those of the former group since we found very little difference in drug levels between the cortex and subcortical regions and traces only in the cerebellum and pons. However, the high levels of the drug found by us in the adrenals suggests that the action of chlorpromazine may be in some way related to the function of the adrenal hormones. Whether a similar relationship can be postulated with regard to lung metabolism remains to be seen, as well as the alternate possibility that the high level of chlorpromazine found in this organ is a result of the chemical structure of the lungs. This is substantiated by earlier observations (Berger, 1957) that different tissues vary in their ability to absorb chlorpromazine.

SUMMARY

1. After the injection of single toxic dosages of chlorpromazine in rats, the highest level of the drug was found in the lungs. Large amounts were also detected in the liver, spleen, stomach, kidney and intestine. The brain contained less than any of these organs.
2. No selective accumulation of the drug was observed in different regions of the C.N.S. of monkeys, although the amount was higher in the brain cortex and basal ganglia than in the spinal cord, cerebellum and pons.
3. Rats injected daily with small amounts of chlorpromazine for periods from two weeks to three months did not contain any measurable quantities of the drug in their tissues. The same was true for liver and brain samples of monkeys injected in a similar way.

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E.C.T. IN SCHIZOPHRENIA

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I. INTRODUCTION

CONVULSIVE therapy as a form of treatment for schizophrenia originated very soon after insulin coma treatment and the induction of convulsions by an electric current was first used by Cerletti and Bini in 1938. For many years insulin comas were regarded as the treatment of choice, although E.C.T. was recognized as having some value, particularly in catatonic conditions. In the last eight years the advent of effective chemical therapy with the tranquillizers has tended to overshadow the value of any other form of treatment.

Nevertheless, an enquiry in 1958 (Baker, Game and Thorpe (1)) showed that E.C.T. was the commonest form of treatment for schizophrenia in the mental hospitals contacted, although insulin comas were still given as the initial treatment of choice by the teaching hospitals. This probably means that at that date the majority of schizophrenic patients (particularly the more severely ill) were having E.C.T. Our enquiry revealed marked individual variation from hospital to hospital in the number of treatments given, and perusal of the common textbooks shows that there is little guidance on this subject, and very little precise research has been conducted. Kalinowsky and Hoch (3) point out that of the published papers on the subject, those which claim the best results always describe longer courses of treatment than those which advise short courses. It is surprising that no attempt has been made to compare the effects of specific courses of treatment, either for their immediate result or influence on the long-term course of the illness.

At Banstead Hospital we have been concerned with the assessment of different forms of treatment for schizophrenia. Initially we compared the effect of insulin comas, E.C.T., and chlorpromazine as initial treatments of choice for schizophrenic illnesses. We eventually abandoned chlorpromazine (Baker, Game and Thorpe (1)) because of the high relapse rate once treatment ceased and many of our patients cannot be relied upon to continue taking any medicine. Later we abandoned insulin comas (Baker, Game and Thorpe (2)) because we found that this treatment had an added risk and far fewer patients commencing

treatment could be expected to complete a course sufficient to give a reasonable degree of recovery. We were therefore left with E.C.T. which had produced a good response in the majority of patients, was safe, and from the point of view of the nursing staff made management easy and enabled us to develop a high morale on the ward. Most of our work had been with a course of twenty E.C.T.s, but following discussion with our colleagues and nursing staff it was thought that this course might be too long and fewer treatments could be used. Clinically, many patients seemed as well after twelve treatments as they were after twenty, and we therefore decided to compare the effects of twelve treatments with twenty. Since those patients having twenty treatments would be in hospital for a longer period than those having twelve, we decided to compare the results of the two different courses given at two different speeds, which we thought would give us some indication whether either the frequency of treatment or the total duration of stay in hospital played any part in the result, as well as the total number of treatments.

II. METHOD

Forty-three consecutively admitted female schizophrenic patients under forty years of age, all of whom had a definite diagnosis of schizophrenia were admitted to the scheme.

Four different courses of treatment were employed. These were as follows:

TABLE I
Distribution of Treatments

Weeks		12 E.C.T.s (Fast)	12 E.C.T.s (Slow)	20 E.C.T.s (Fast)	20 E.C.T.s (Slow)
1	..	5	3	5	3
2	..	3	3	3	3
3	..	3	2	3	3
4	..	1	2	3	3
5	..		1	2	2
6	..		1	2	2
7	..			1	2
8	..			1	1
9	..				1

The Ectonus technique was used—patients receiving from 3 to 6 grains of sodium amytal one hour preceding treatment. Anaesthetics and/or relaxants were rarely used (only about one patient in ten).

Patients were allocated to treatment groups by a random selection procedure once it was decided that they were physically fit.

Assessment of Patients

All patients were rated on the Wittenborn Rating Scale (Wittenborn and Lesser (4)) immediately preceding treatment and again one week following their last treatment. The ratings were carried out by the ward doctor.

One week after completion of the course of treatment the consultant decided *on clinical grounds* whether the patient was fit for discharge. Most of these patients who were considered to be unfit for discharge following a course of twelve treatments were then given eight more E.C.T.s to make a course of twenty.

III. RESULTS

The results of treatment in terms of discharge rates are set out in Tables II-IV.

TABLE II

Results of Treatment—Discharge Rates
(Percentages in brackets)

		Treatment			
(a) <i>All Groups</i>		12 slow	12 fast	20 slow	20 fast
Admitted to scheme	..	14	10	7	12
Patients discharged following treatment	..	3 (21·5)	4 (40·0)	5 (71·5)	8 (66·5)
Patients discharged on drugs following treatment		0 (0·0)	1 (10·0)	1 (14·3)	0 (0·0)
Total discharged after treatment		3 (21·5)	5 (50·0)	6 (86·8)	8 (66·5)

		Treatment		
(b) <i>12 v. 20 E.C.T.s</i>		12 E.C.T.s	20 E.C.T.s	CR.
Admitted to scheme	..	24	19	—
Patients discharged following treatment	..	7 (29·0)	13 (68·5)	2·97**
Patients discharged on drugs following treatment		1 (4·2)	1 (5·3)	<1·0
Total discharged after treatment		8 (33·3)	14 (74·0)	2·94**

		Treatment		CR.
(c) <i>Fast v. Slow Course</i>		Fast	Slow	
Admitted to scheme	..	22	21	—
Patients discharged following treatment	..	12 (54·5)	8 (38·0)	1·1
Patients discharged on drugs following treatment		1 (4·5)	1 (4·5)	<1·0
Total discharged after treatment		13 (59·0)	9 (43·0)	1·06

* Statistically significant at the 5 per cent. level.

** Statistically significant at beyond the 1 per cent. level.

TABLE III

Critical Ratios for Differences Between Four Treatments

		Treatment			
Treatment:		12 Slow	12 Fast	20 Slow	20 Fast
12 S.		()	1·4	3·9**	2·6*
12 F.			()	1·8	<1·0
20 S.				()	1·1
20 F.					()

TABLE IV

Results of Treatment for Patients not Responding to 12 E.C.T.s and Continuing to 20 E.C.T.s

(Percentages in brackets)

	Original Treatment Group		CR.
	12 Slow	12 Fast	
Number of patients failing 12 and continuing to 20	9	5	
Patients discharged following 20 E.C.T.s	3 (33·3)	2 (40·0)	<1·0

The results of treatment in terms of Wittenborn standard scores are set out in Tables V-X. The Phobic Compulsive and Conversion Hysteria scales have been omitted.

TABLE V

Wittenborn Means Before Treatment

[illegible]

TABLE VI

Wittenborn Means After Treatment—All Patients

[illegible]

TABLE VII

Wittenborn Means for Patients Discharged One Week Following Treatment

[illegible]

TABLE VIII

Wittenborn Means for All Patients After Their Course of Treatment: 12 v. 20 E.C.T.s

Treatment	Paranoid Schizophrenia	Paranoid Condition	Schizophrenic Excitement	Hebephrenic Schizophrenia	Depression	Mania	Anxiety
20 E.C.T.s N=17 ..	2.1	1.3	1.9	1.5	2.7	1.6	1.2
12 E.C.T.s N=22 ..	2.9	1.7	2.4	2.0	3.2	1.6	1.5
CR. ..	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

TABLE IX

Wittenborn Means for All Patients After Their Course of Treatment: Fast v. Slow Course

Treatment	Paranoid Schizophrenia	Paranoid Condition	Schizophrenic Excitement	Hebephrenic Schizophrenia	Depression	Mania	Anxiety
Fast Course N=20 ..	2.1	1.3	2.1	1.8	2.2	1.8	1.1
Slow Course N=19 ..	3.0	1.7	2.2	1.6	2.7	1.4	1.5
CR. ..	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

TABLE X

*Wittenborn Means for Patients Failing to Respond to 12 E.C.T.s and Continuing to 20
Mean Scores Before Continuation of E.C.T. in Brackets*

Treatment	Paranoid Schizophrenia	Paranoid Condition	Schizophrenic Excitement	Hebephrenic Schizophrenia	Depression	Mania	Anxiety
12s. N=4	3.7 (4.2)	2.0 (2.3)	1.8 (2.3)	1.0 (1.8)	1.0 (3.0)	1.2 (1.0)	1.7 (2.0)
12f. N=4	1.5 (4.4)	1.5 (2.0)	1.5 (3.0)	1.0 (3.0)	1.7 (3.8)	1.2 (3.0)	1.0 (1.2)
CR. ..	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

IV. DISCUSSION OF RESULTS

We must emphasize that the patients in this scheme would be considered to have a bad prognosis on the usual criteria. They have often had previous treatment with the tranquillizers, and as noted in our other papers, may be socially isolated.

The significant finding in this research is shown in Table II. This shows that twenty E.C.T.s are more likely to lead to the patient's discharge than twelve E.C.T.s. The other tables show that the differences between the rate at which treatment is given are not significant.

The patients were discharged if they seemed well enough on clinical and social grounds. We must consider whether this decision was biased, either by a desire to discharge patients as quickly as possible or by a preference for one or other course of treatment. The Wittenborn scores before treatment show no significant differences between the four groups. Similarly, the scores after

treatment show no significant differences. Nevertheless, if we look for evidence of bias, we can see in Table VII that in general the patients having twelve E.C.T. who were discharged had fewer symptoms than those who had twenty E.C.T. and were discharged. However, not only are these differences not significant, but if we look at Table VI it can be seen that the patients having twenty treatments as a whole had fewer symptoms than those having twelve treatments.

Lastly, Table X is included to show that those patients who received twelve treatments and subsequently a further eight, did have more symptoms than those discharged after twelve, and fewer symptoms when twenty had been completed.

V. SUMMARY

This present research shows that female schizophrenic patients under forty, who are admitted here will have fewer symptoms after a course of twenty E.C.T.s than after a course of twelve and their likelihood of discharge is significantly improved. It is essential to note that the treatments have been given by the same team of doctors and nurses in an atmosphere of therapeutic hope and a very active social and rehabilitation programme. We do not believe that twenty E.C.T.s is necessarily the ideal course of treatment for the schizophrenic patient, but do believe that further research is essential, in particular an adequate "follow-up" study.

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PSYCHOLOGICAL EFFECTS OF STEREOTAXIC OPERATIONS FOR THE RELIEF OF PARKINSONIAN SYMPTOMS

By

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IN view of their many inter-connections with the cortical grey matter, the effects of lesions in the basal cerebral nuclei are of the greatest theoretical interest. On account of the rarity of naturally occurring lesions confined to these nuclei, there have been few reports of psychological changes in patients with discrete subcortical lesions. Smyth and Stern (1938) described four cases of intrinsic tumour of the thalamus, all of whom gave evidence of organic dementia early in the course of the disease. Eaton *et al.* (1939) reported six cases of symmetrical cerebral calcification preponderating in the basal ganglia, with no radiographic evidence of cerebral atrophy, of which the clinical concomitants included mental retardation. Alford (1948) has gone so far as to insist that destruction of thalamic nuclei is alone responsible for intellectual impairment, and that "focal" defects associated with different cortical lesions are related either to sensory disturbances or to the psychiatric state of the patient.

Experimental subcortical lesions in animals have been associated with changes in performance, though it is questionable to what extent these results are applicable to man. Lashley (1945) investigated the nature of inter-action between different regions of the cortex in the rat by making incisions in the cortical surface, dividing long association tracts. In those animals in which under-cutting of the white fibres resulted in thalamic degeneration, he found a remarkably close association between amount of impairment on maze learning and amount of thalamic degeneration. An experiment which has a more direct bearing on the present study is that of Rosvold *et al.* (1958) involving stereotaxic subcortical lesions in monkeys. The authors noted that "the behavioural deficits which follow certain neocortical ablations in the monkey have not been produced by placing lesions in the thalamic nuclei which project to these neocortical areas". They found that single alternation performance was impaired by caudate-nucleus as well as by thalamic and splenic lesions, and suggested that "a complex and widespread anatomical system rather than a simple and localized one may be involved in successful alternation performance".

The most comprehensive study of the effect of subcortical operations in man on psychological test scores is the study of Riklan *et al.* (1960). Describing the changes in scores on the Wechsler-Bellevue scale of eighty-nine consecutive patients tested a few days before chemopallidectomy or chemothalamectomy and retested within a month after operation, they state that "both the left and right brain groups evidence significant decreases in Verbal and Full Scale I.Q. scores, but only the right brain group demonstrates a significant decrease in Performance scores. Analysis of the subtests indicates that Digit Span is the one most affected, primarily for left brain cases. Trends indicate that the left brain group show greatest decline in Similarities, Picture Completion, and

Digit Symbol tests, while the right brain group is more affected in Picture Arrangement". Elsewhere the authors state "for the left brain group, the three subtests most affected are the Digit Span, Arithmetic, and Digit Symbol tests. For the right brain group, they are the Picture Arrangement, Block Designs, and Object Assembly tests". They also note that there is a significant relationship between impairment of "expressive language functions" (presumably degrees of dysphasia, though no criteria are stated) and Verbal I.Q. loss; and that, apart from laterality of lesion, there are no significant differences in results between lesions in the globus pallidus and in the thalamus, except for slightly greater Verbal I.Q. loss with left-sided thalamic lesions. In forty-nine patients retested about nine months post-operatively, these deficits were no longer in evidence, and there was some slight increase in Performance I.Q. in the group operated on the left.

PRESENT STUDY

The patients represent all those selected for subcortical operation for the relief of unilateral Parkinsonian symptoms who had been referred for psychological testing at the time of writing. There were seventy in all, but four of these were too incapacitated to be able to do any tests. Table I summarizes the results

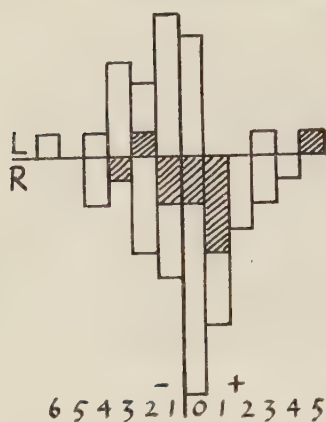
TABLE I
Mean Pre-operative Scores of Patients

Operated Side	Age	No.	Digit Span	Arithmetic	Similarities	Vocabulary	Picture Completion	Picture Arrangement	Blocks	Sentence Learning	Memory for Designs
Left	49.2	40	1.2	1.1	1.2	1.8	1.9	-1.3	-1.1	10P/4F	2P/4F
Right	52.4	26	0.8	0.7	1.2	2.2	1.6	0.1	1.0	9P/12F	1P/8F

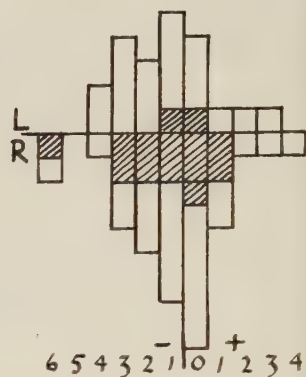
of pre-operative testing on subtests of the Wechsler scales and on Sentence Learning (Zangwill, 1943) and Memory for Designs (Terman and Merrill, 1937). Results on the Wechsler subtests are presented as the means of individual differences (in scaled score points) from the mean score appropriate to the patient's age in the case of the Wechsler-Bellevue scale (Wechsler, 1944, p. 222), or from a mean score of 10.0 using age-scaled scores in the case of the W.A.I.S. The sentence learning test was passed if the patient required not more than five repetitions to learn the sentence to two correct consecutive repetitions; and memory for designs was scored according to IX-year standards, with the proviso that the examiner himself drew the designs, and allowed the patient to study them for as long as he wished before attempting to reproduce them. The patients are grouped according to the side subsequently operated on.

The significance of differences between means has been tested by calculation of "t", and of differences between proportions by the χ^2 method. In view of the large number of these statistics computed, the significance of the difference is not regarded as established unless the statistic exceeds the $p = .01$ level of probability. None of the differences between the groups in the results in Table I is significant at this level: the most significant difference is that of 2.1 points on the Block Designs scores between those with left and those with right-sided operations which, with $t = 2.15$, $.02 < p < .05$, may be regarded as suggestive.

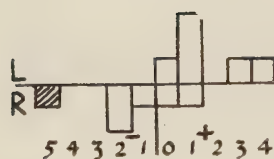
Fifty-six of these patients were made available for retesting, on the same tests as pre-operatively, as soon as they were "up and about", and in any case not more than four weeks after operation. The distributions of differences, in scaled score points, between pre- and post-operative results on five of the



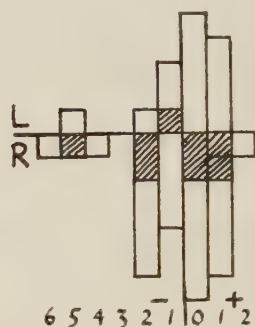
(a) Digit Span



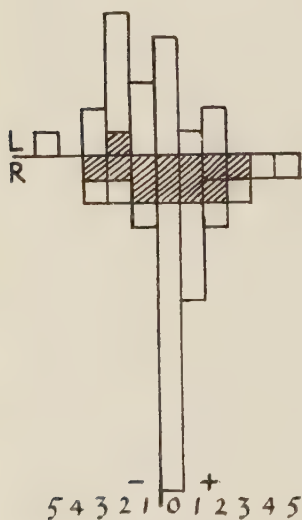
(b) Arithmetic



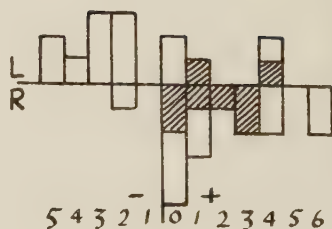
(c) Picture Arrangement



(d) Block Designs



(e) Similarities



(f) Sentence Learning

FIG. 1.—Changes in test scores following subcortical operation. In (a)–(e), the units reading horizontally are scaled score points; in (f) they are changes in number of repetitions required to learn the sentence, with sign reversed. The vertical dimension represents the numbers of patients: above the line, those operated on the left; below, those operated on the right. Cross-hatching represents thalamic operations.

subtests is shown in Figure 1, *a-e*, and the distribution of changes in numbers of repetitions needed to learn the sentence is shown in Figure 1, *f*. It will be noted that in nearly all groups, the distributions approximate to normality in shape. The patients have been subdivided according to side of operation, and those who underwent chemothalamectomy (McCaul, 1959) are represented by cross-hatched squares: the remainder underwent electrical thermocoagulation aimed at the globus pallidus (Mr. L. S. Walshe).

Table II shows the mean change in scores of each group of patients,

TABLE II
Mean Changes in Scores After Operation

Side of Operation	Digit Span	Arithmetic	Similarities	Vocabulary	Picture Completion	Picture Arrangement	Blocks	Sentence Learning
Left	-1.2*	-1.2**	-1.2**	-1.0*	-0.7	1.7*	-0.4	-1.7*
Right	0.3	-0.9*	0.4	-0.1	0.1	-1.5	-0.9*	1.7*
Between groups ..	1.5*	0.3	1.6***	0.9*	0.8	3.2**	0.5	3.4***
Total number ..	56	54	50	49	43	12	40	28

Levels of significance of "t" are indicated by asterisks: *, $p < .05$; **, $p < .01$; ***, $p < .001$

and also the difference between these means: the level of significance is indicated of the difference between mean pre- and post-operative test scores for each group, and of the difference between groups in the change in scores.

It will be seen that there are significant differences in post-operative change between those operated on the left and on the right on Similarities, Picture Arrangement, and Sentence Learning, and a suggestive difference on Digit Span and Vocabulary. On the four verbal tests, this is associated with greater impairment following left-sided operation, while on Picture Arrangement there is improvement in those operated on the left and deterioration in those operated on the right. On Arithmetic and on Block Designs, there is impairment after operation in both groups; it is greater on Arithmetic following the left-sided operation, and greater on Block Designs following the right-sided operation.

In view of the statement of Riklan *et al.* (loc. cit.) that pre-operative mental impairment is related to immediate post-operative intelligence loss, we have examined the post-operative results in relation to the patients' abridged Deterioration Quotients (i.e. discrepancy between Vocabulary and Picture Completion, and other subtest scores). Comparison showed that approximately equal proportions of those with and without pre-operative deterioration showed post-operative increase, decrease, and no change in scores.

In eight of the patients operated on the right the personality change after operation was sufficiently striking to have been manifested during testing; but in only one of those operated on the left. The change was generally in the direction of euphoria, not unlike the change seen after leucotomy, but in one of the eight it was mildly depressive. In view of the relatively small numbers of those seen after chemothalamectomy, we have not examined the differences in results between them and those who underwent operation on the globus pallidus: the distribution of their scores, shown in Figure 1, appears to be much the same as those of the globus pallidus group.

DISCUSSION

Comparison of the pre-operative test scores of our patients with normal averages (Table I) shows that, while Vocabulary and Picture Completion scores were, on average, nearly 2.0 scaled score points above the normal mean, scores

on all other tests were considerably below this level. In terms of Wechsler's Deterioration Quotient, this indicates a significant degree of deterioration in the majority of patients before operation. The principles underlying Wechsler's method of estimating deterioration have been supported in a study of patients with localized, mainly cortical, cerebral lesions (McFie, 1960), in which it was demonstrated that, while Vocabulary and Picture Completion scores appeared to be relatively unaffected by cerebral lesions, scores on other tests were selectively affected by lesions in different locations. Compared with the average patterns of deficit found in cases with cortical lesions in different lobes, the distribution of deficits shown by the present series of patients before operation suggests widespread rather than focal intellectual impairment; and this agrees with the observation on ventriculography for location of the stereotaxic instrument, that many patients had slightly dilated ventricles. Exceptional results are those of the patients with right-sided symptoms, whose scores on Picture Arrangement and on Block Designs were rather lower than those of the contralateral group. This is particularly unexpected in view of the fact that in this group it may be presumed that the cerebral lesion is largely left-sided, yet the impairment is most marked on "performance" tests, which are usually most sensitive to right-sided lesions. The explanation probably lies in the fact that the impairment is related not to the cerebral lesion but to the peripheral symptoms, disturbances of movement of the right hand resulting in greatest impairment on performance tests.

Comparison of our post-operative results with those of Riklan *et al.*, shows a considerable amount of agreement. The average age of their patients was very similar to that of ours, and the conditions and time intervals of testing were almost identical with ours. Under these circumstances, it is very encouraging to observe the similarity of results in the two series. In general, the effect of the left-sided operation is a lowering of scores on verbal tests, while that of the right-sided operation is to lower "performance" scores. The findings of Riklan *et al.*, indicate some impairment on Digit Span following right-sided operation: we have not found this in our patients, but for all the other subtests we have been able to confirm their observations.

Changes in test scores after operation may be the result of a number of influences. Some will tend to lower scores, e.g. intellectual or emotional impairment consequent upon the lesion, and possibly impairment of motor control (though this is a rare complication). Others may result in improved scores, e.g. improvement in motor control, personality change of a beneficial kind, and practice effect (if the same test is used in retesting). Evidently, the increases in scores after operation (on Picture Arrangement in the left group and Sentence Learning in the right group) must be the consequence of changes of the latter kind. Improvements in motor control would not improve scores on these tests; and as Riklan *et al.* have suggested conditions are hardly favourable for the establishment of practice effects. This suggests that personality change may be the major influence, and certainly a large number of patients show improved emotional reactions following alleviation of their symptoms. Losses, however, are almost entirely the consequence of the operative lesion, and it is of interest to compare the results with those of lesions in the cortical surface. Riklan *et al.* did not compare their results with published data on the effects of lesions in other parts of the cerebral hemisphere: they consider that "the immediate post-operative losses . . . suggest interference with the more immediate mobilization of mental energy required for learning and integration", and that "the condition of the altered physiologic milieu,

rather than the anatomic damage itself, seems to be of primary importance".

The differences between changes following left- and right-sided subcortical operations resemble closely the differences between effects of left- and right-sided cortical lesions (cf. Anderson, 1948; McFie and Piercy, 1952). As the damage done by the stereotaxic instrument on entering the cerebrum is slight, these changes must be the consequence of the subcortical lesion. It is perhaps not unexpected that thalamic damage should result in some intellectual impairment; but the evidence that similar impairment follows a lesion in the corpus striatum suggests that its functional relationships are not entirely restricted to the motor systems. Furthermore, in the present series of patients the tests on which there is the greatest impairment following the left-sided operation are Similarities, Arithmetic, Digit Span, Sentence Learning and, to a slight extent, Vocabulary; while following the right-sided operation these are Picture Arrangement and, to a slight extent, Block Designs and Arithmetic. If these patterns of impairment are compared with those commonly found in association with lesions in the cerebral lobes (McFie, loc. cit.) it will be seen that they resemble most closely the deficits found with lesions in the left and right temporal lobes. On the face of it, this appears surprising, since the cortex of the temporal lobes receives no direct projections either from the globus pallidus or from the nuclei of the thalamus, which are the targets of the stereotaxic operation. However, recalling the findings in monkeys of Rosvold *et al.* (loc. cit.), it may be that functional relationships between the cortex and subcortical nuclei are more complex and widespread than would be suggested by their direct anatomical connections.

SUMMARY

Subcortical stereotaxic operations for the relief of Parkinsonian symptoms provide an opportunity for the study of psychological changes following lesions in these nuclei.

Fifty-six patients have been tested before and soon after unilateral operation aimed at the globus pallidus or the ventrolateral nucleus of the thalamus. The changes observed are losses on verbal tests following operations on the left and on "performance" tests following those on the right. These results are similar to the types of impairment found with cortical lesions in the same hemispheres.

The significance of these losses, and of certain gains in scores, is discussed.

ACKNOWLEDGMENTS

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JUNG'S "ARCHETYPES" AND PSYCHIATRY*

By

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THE "archetype" is a concept of Jung's which is fairly widely accepted as a valuable one in spheres of art, literature and theology. Few psychiatrists seem to know much about the concept, and of the few who are interested in it, most find little relevance in it for their clinical work.

There is still a tendency today to regard the theories of analytical psychology as vague and mystical, and perhaps this is inevitable. Jung's output of original ideas has been prodigious, his writing is often obscure, apparently contradictory and difficult to relate to immediate problems of clinical practice, and the task of working out the clinical application of his ideas is still in its infancy. Despite these disadvantages analytical psychologists claim that they provide a useful and unique approach to the problem of mental illness. Much of this paper which stems from this approach will not be new to many psychiatrists, and will, I think, conform to the views of some psycho-analysts, who would use different terminology.

My thesis is that there exist, within the individual, forces which work in the direction of healing and growth, that these are as real and vital in the psychic as in the organic sphere, and that this view has important implications for the psychiatrist.

There is nothing novel in this idea, which is acknowledged in the familiar statements about the healing power of time, the healing forces of nature and in the concept of maturation, but the justification for enlarging on it is that analytical psychologists having special interest in it have made contributions in theory and practice to the understanding of synthetic forces in the psyche. Jung's view of neurosis is that it represents an attempt by the individual at achieving a more mature level of adaptation, and although the attempt may be more or less unsuccessful it has a highly positive significance. A corollary of this view is that the psychopathological components of the neurosis (in psycho-analytical terminology *the infantile sexual contents*), are not necessarily causal, although they may be explanatory. A further implication is that therapy should consist of a process of creating the conditions within which the synthetic forces in the psyche may become freed from the automatically repeating neurotic patterns which are based on unconscious fantasy. It is in the unconscious fantasies that the synthetic forces are to be found and when these forces become free, either in the course of normal growth or of successful therapy, dynamic changes occur within the individual which lead to a greater unification of his divided and conflicting parts. This last statement is crucial to my theme.

I do not think that this view of therapy is essentially different from that of

* Based on a paper read to the Psychotherapy and Social Psychiatry Section of the Royal Medico-Psychological Association, 12 November, 1959.

many psycho-analysts today. It is based on the idea of an inner world containing, among other things, psychic contents* which tend to behave as subordinate personalities with a life of their own, more or less divorced from the control of the individual ego. It is a view that Jung has held to since the early days of psycho-analysis, and one might say that it is essentially an introvert's view of the psyche. At any rate, Jung seems to have felt this, and it has been his concern for such introverted matters as values, meaning and purpose that have led him to criticize the classical Freudian approach as rigid, mechanistic, "merely explanatory" and failing to do justice to the complexity of the individual. Today, when the idea of an inner world is more widely accepted, many of Jung's criticisms seem more than a little out of date.

However, despite the increasing common ground that is appearing between analytical psychologists and many psycho-analysts it would be facile and misleading to under-emphasize the dissimilarities, as they are so vital, and I shall have occasion to point some of these out.

My statement about the ideal of therapy contains the idea of a situation being created in which the parts of the individual may come together. This situation is the transference, and the process was vividly described by Dr. Sutherland when he and Dr. Fordham (4) addressed the Psychotherapy and Social Psychiatry Section recently on the analytic approach to the care of patients. He said "We have often to see these conflicting parts not as a kind of abscess to be drained from a healthy organ, but as highly complicated structures, capable almost of acting like separate people in their powers of perceiving the world as they need to see it and to manipulate people into the roles they need." Regarding the situation within which these parts may come together he says that when the patient feels he is being understood and accepted he feels this as a "longed-for safety situation in which he can bring his conflicting parts together". Later he talks of therapeutic interpretations as comments from the doctor which bring the conflicting parts together. Here it is worth while pointing out a difference in views: whilst an analytical psychologist would agree with Sutherland's admirable description of the situation, he would not agree that either the doctor's words or the patient's ego are solely responsible for bringing the conflicting parts together. Basically he sees this sort of synthetic process as originating in the non-ego and requiring for its comprehension such an idea as Jung's concept of the self. This refers to what has been called, rather vaguely, "the whole man", and is to be distinguished from the psycho-analytic concept of the self† as the subject's awareness of himself as an object. Jung's "self" is an idea he found necessary to do justice to what he saw as powerful forces within the psyche, tending towards producing a state of wholeness. By "wholeness" is meant an amalgam of conscious and unconscious contents without regard for the current workings and orientation of the ego. If the ego is too vulnerable a psychotic disintegration can be the outcome of such an activity. This difficult and elusive idea has been brought more into relation with clinical practice by Fordham's (2) theory of deintegration of the self. This idea, which I shall only touch on, embraces more fully the dynamics of the phenomena subsumed under the concept of the self, and relates them to ego development. In these terms, the much disputed "death instinct" would be

* "Psychic contents" is a conveniently general abstraction which embraces such related concepts as "internal objects and part objects" (Klein), "unconscious complexes" and "archetypal images" (Jung), and "dynamic structures" (Fairbairn).

† The psycho-analytic "self" has not yet been satisfactorily defined and at times is used in a way which seems to suggest an attribute of "wholeness", as in Jung's "self".

seen as an expression of an innate tendency towards breaking down of the ego's current boundaries, and it is held that without this rhythmical breaking down and subsequent reforming and renewal there can be no development. The ultimate effect of the activity of the self, once a mature ego is established, is to influence the subject in such a way that he gradually renounces the idea of his ego as the centre of his psychic organization, which is felt more and more to shift into the non-ego. When this state of affairs is dealt with by projecting the archetypal contents, a traditional religious attitude may result. By "traditional" I mean a vital state in which the objects of religious attention are powerful and alive for the subject and his life is centred on them and changed by them.

When these contents are not projected, a rather different process of development may occur, which Jung has termed "individuation". The two outcomes are not necessarily mutually exclusive. "Individuation" in a technical sense involves the ego adopting a particular sort of attitude towards the contents, which has been called the "symbolic attitude". This means that the subject is able to observe these images as well as to experience their effect on him. This is sometimes elaborated as a technique of introspection, called "active imagination". The experiential aspect of this process could perhaps be called "religious", whilst the observational aspect and the exploratory motive have something in common with science. A somewhat similar notion of experience and observation combined has appeared in psycho-analysis in the idea of the analyst as "participant observer".

Such development seems to be within the capacity only of reasonably mature subjects and so forms a relatively small part of the analyst's clinical experience. "Individuation" or the full integration of the personality could be called an unattainable ideal or goal, and it is meant to express a process of continuous development that ends only with death. This process is not the exclusive prerogative of the analysand, but is related to what is generally seen in the person who goes on living a productive and increasingly mature life.

Stated baldly like this, these concepts are at once open to all sorts of misinterpretation. On the other hand they may be dismissed, as they often are, as unscientific mysticism. Here the pejorative connotation of these terms "unscientific" and "mysticism" contains a lot of dubious presuppositions about the nature both of science and mysticism which usually go unquestioned. Confusing words no doubt contribute to this frequent protest. "Collective" for instance, in the "collective unconscious" idea, is sometimes taken as implying some sort of amorphous group mind, whilst "transpersonal" may be misunderstood as implying a phenomenon that in some way is not personal, even "other-worldly" (cf. Jackson (5)). At the other extreme these ideas may be so idealized that the images of the unconscious become endowed with such prestige that it is but a short step to a cult-attitude. An attitude between these extremes will see these concepts as important instruments for present understanding and future research, despite the fact that they are so hard to pin down precisely. It is worth remarking here that the self is not merely the hobby-horse of analytical psychology, and that psycho-analysts have attempted to systematize similar phenomena into concepts which appear to be related. Winnicott's (7) "psyche-soma" and Clifford Scott's (6) "body scheme" are examples.

This rather large and lightning excursion into theory illustrates one important aspect in which the approach of analytical psychology does not agree with traditional psycho-analytic theory. My earlier point of difference, and one more germane to the rest of my paper, is the positive attitude taken by analytical psychology towards neurosis, as a more or less frustrated achievement.

This earlier idea could be dismissed as a rationalization produced for the comfort of patients, but it rests on solid observational grounds. This so-called "prospective" view of neurosis does not mean that neurosis is a good thing, or that the neurotic subject is a genius *manqué*, but rather that in the neurotic subject who comes into analysis the synthetic forces are more readily discernible than in the so-called "normal". Because it is in the imagery of dream, fantasy, vision or hallucination these synthetic processes can be detected, something must be said about imagery before I can proceed to the question of what relevance all this has to general psychiatric practice.

Jung detected in such imagery certain regularly recurring patterns or motifs resembling in their forms mythological themes usually involving human or animal figures behaving in specific ways, and associated with a subjective experience of powerful affect. That is to say that the individual feels them as important and impressive, the impression may remain with the subject for hours, years or even a lifetime, and the meaning of the experience may only gradually unfold over a very long time, if at all. These are the primordial or archetypal images and the archetype is the concept contrived to explain the phenomenology of this class of imagery. Archetypes, then, are theoretical entities, "psychoïd" in nature. The concept implies a physiological basis to the phenomena*, and thus is in some ways similar to that of instinct, but it is more embracing in that the archetype is held to express itself both in bodily experience and in mental images. A similar idea has appeared in the psycho-analytic theory of the Kleinian group, which holds that unconscious fantasy is the mental representation of instinct.

Neurotic symptoms, then, result from unconscious fantasy and the defensive compromises to which it is subject; and unconscious fantasy is activated when the individual fails to adapt adequately to his life. For Jung, the libido is not exclusively sexual, but undergoes a variety of transformations in the course of development from nutritional to presexual, to sexual and ultimately to spiritual forms. At the points of development where adaptation fails fantasy develops, and it is to these points that the subject may later regress when development comes to a standstill and a neurosis is established. In conformity with the ideas of a growth-promoting tendency, the self, Jung sees this regression as a potentially integrating and healing one, a return, as it were, to pick up the bits that have been left behind. One can see here resemblances to the psycho-analytic idea of "fixation points", but modified into "points of potential growth". It is at these points where fantasy occurs that the archetypal processes can become active and it is in this sense that Jung holds that infantile sexuality need not be of causal significance in neurosis. In practice this means that there are some neurotic subjects who will only get well if they are enabled to regress to these growing points within the transference relationship. We shall return to this later when touching on the question of the natural history of neurosis. A question that must be answered is "By what right are these forces called 'synthetic'?", and the answer is that it is a matter of observation of subjects in analysis. The neurotic analysand has a relatively impoverished capacity for object relationships, and if he has a successful analysis these improve, and his neurosis diminishes or disappears. During the course of analysis he can be seen to change and the change is brought about by the freeing of unconscious contents previously bound in his symptoms and neurotic

* Fordham (2) has pointed out the similarity of the function of the archetype in perception to that of the Innate Release Mechanism postulated by Ethology.

patterns which become available to his ego in a useful form and thereby enrich it.

Most of the foregoing concepts are what I would call large-scale or macroscopic ones. At first sight they seem to have little in common with the intricate and elaborate formulations of Freudian metapsychology. They may be of little help in the unravelling of the detailed dynamics of behaviour and they tell us next to nothing of the intricacies of the defensive manoeuvres of the ego which are clearly illuminated by psycho-analytic theory. On the other hand they do offer a view of the meaning of neurosis, and a system to which other concepts both biological and psychological may with profit be related.

And this is where I feel that the foregoing has relevance for the psychiatrist. In the above view neurosis is anything but a disease in the traditional sense of medicine. The view of neurosis as a disease, with the attendant view of symptoms as morbid phenomena to be extirpated with all possible despatch is, it seems to me, widely held in medicine, at least in this country, and I have met few general physicians who do not hold to it uncritically.

This view of symptoms as evil is not confined to general medicine and does, I believe, inform and motivate the approach of many psychiatrists, who thereby tend to be assailed by the *furor therapeuticus*, sometimes to their own despair and to their patients' detriment. However, the prospective view of neurosis implies that with some patients refraining from treating them, in the sense of removing or trying to remove their symptoms, is not merely a matter of *laissez-aller* and having a thick skin, nor a pious hope that they will get better at coping with their disability. On the contrary it confronts us with the demand to find out much that we do not yet clearly know. Is it true, as Sutherland states, that given a "safety situation" and being offered this situation at critical times for a very long period if necessary, some people will achieve much more than merely coping better with their difficulties? In my experience of this problem it is indeed true, and much research remains to discover just what the "safety situation" required is, how it can best be supplied, by whom and to whom. This view implies that the traditional "supportive clinic" might be made a very much more dynamic and therapeutic affair than it often is.

The prospective view of neurosis seems to me to bring psychological disorders more into line with organic disorders, however different they may be in other respects. If the physical organism has its maturational and defensive-repair processes, its compensatory reactions, its inflammations and immunological responses, why should it be so difficult to envisage the psyche as having similar functions of repair and growth? Just as the fever is not the infective process nor the repair process in itself, but is an overt sign of the activity of the underlying invasion-healing process, in the same way the neurosis can be regarded as not the healing process nor the pathological process itself, but as an overt sign of an underlying invasion-healing struggle.

(Many people are drawn to the "disease" view of psychological disorder by the evidence of genetics, physiology and biochemistry and the response of certain syndromes to specific measures of physical therapy. Indeed there seem to be advantages in viewing at least some syndromes as nosological entities. When we turn our attention to the biological correlates of mental disorder we find a range of states, from neurosis, where biochemistry and physiology are not usually held to be of great aetiological relevance, to psychotic and primarily organic disorders, where chemical and other processes are widely held to be of considerable aetiological significance. Despite the importance of chemistry and physiology in these states the prospective view may none the less be relevant.

For the subject of, say, a recurrent epileptic confusional state, his object relationships may well be as important for the understanding of his condition as his temporal lobe focus. We should remember that although we find it virtually impossible to think in other than dualistic terms, the body fundamentally knows no such dualism. It seems that there is a level of mental life in which chemical change and affect follow on perception without priority of one or other. The concept of the archetype represents one attempt to bridge this gap in our thinking, in so far as it embraces bodily change on the one hand, and perceptual imagery and affect on the other.)

Holding to the view that neurosis is not a disease process, I should like to emphasize how little we actually know of the natural history of neurosis. There seems to be an increasing interest in this subject nowadays, and there is evidence to suggest that neurosis tends, in a large proportion of cases, to spontaneous cure. What this "cure" may represent we shall return to shortly. If this be true, it complicates assessment of our therapeutic endeavours considerably. When a patient apparently recovers after say, chlorpromazine therapy, or brief psychotherapy, we tend to be gratified, reassured about our potency and impressed by the efficacy of our approach. Such an event may represent a confirmation of our prejudices which is entirely illusory. Control techniques, in so far as they are possible, may help to avoid this illusion in the case of drug therapy, but the same cannot yet be said of minor psychotherapy. Is it not likely that in a number, perhaps the large proportion of such cases, what really happens is that we help to reduce the patient's anxiety and then witness a spontaneous recovery? This would imply that when such therapy works, it does so in a manner analogous to the sulphonamide that holds the situation while the healing mechanisms do their work.

Experience shows that many spontaneous "cures" consist of a reorganizing of psychic forces, a restructuring of defences, without any evidence of growth, in the sense of improvement in object relationships. Often such a process can be considered as a successful social adjustment, but however beneficial that may be, it is not valued very highly by the analyst who has the "whole man" in view. Although this comment may sound like an idealization emanating from the ivory tower of an analyst's consulting room, it expresses the point of view that the uncritical acceptance of social adjustment as a good thing for the patient may proceed to a mechanistic "fitting the patient into society" approach which has very important implications, both individual and social. Some of these have been elaborated by Bion (1), Fordham (3) and others.

Not all spontaneous "cures" however, are likely to be of this nature, and those in which something more than mere readjustment is achieved are particularly important. When we know more about these matters we will be in a better position to say what sort of aid should be offered to patients at what time. Perhaps we will sometimes need to wait for the crises before even offering help, if only because some people seem to be receptive to change only at these times. The principle of offering "treatment" to all comers is an unsound one. It is a common enough experience to find a patient breaking off psychotherapy after a few sessions, only to return in months or years when they are as it were, "ripe" for it.

Recovery from neurotic and psychotic states is probably a highly complex matter, whether it be achieved chemically, electrically or psychotherapeutically. We know something about the way patients fall ill, but less about how they fall well. Falling well involves the establishment or re-establishment of object relationships and I think that analysts may reasonably claim to be the only

people in a position to say much about these complex dynamic processes. Even if what they have to say at the moment may be little, it is, nevertheless, a start.

If neurosis is not a disease, and symptoms are not essentially morbid phenomena, what may they represent, more specifically, in the individual case? One view is that many symptoms, particularly hysterical and phobic ones, can be seen as warning signals to the individual that something is wrong in the way he is conducting his life. This sounds a little naïve and animistic, but experience shows that it is sometimes a perfectly valid attitude to the symptom. When treatment is successful in such a case, the symptom can be viewed in retrospect as the clamour of psychic contents which can no longer go on being ignored. These contents may represent, say, a neglected marriage problem or a failure to fulfil a latent potentiality, and the symptoms may not disappear until this underlying demand is fulfilled.

The same is sometimes true in the case of depressive symptoms. It is known that severe depressive states are associated with late middle and old age. The reason for this is unknown and many investigators look in the direction of hormonal and genetic processes for enlightenment. From this point of view of the "whole man" a possible factor emerges. This is that this group contains those people whose development throughout life has been what Jung calls "one-sided", who have failed to meet the more introverted demands of the second half of life, and who therefore view approaching age with dread. In the psychotic depressions of this period the fear of death as abandonment, loss and separation may activate depressive mechanisms established at a very early or constitutional level, where physiological and biochemical processes may participate.

Although there is not complete agreement about the psychopathology of depression, it is widely accepted as a phenomenon arising from the threat to the love object offered by the destructive aspect of the subject's ambivalent attitude. In these terms much of what is loosely called "depression" in clinical practice is better understood as states of hopelessness about object relationships and of schizoid futility. By contrast to these, what one might call a "true" depression needs sometimes to be seen as an achievement. In his masterly exposition of the Kleinian theory of the depressive position, Winnicott (8) emphasizes the way in which the capacity for concern grows as this position is attained. Analysts often feel considerably gratified when certain of their patients begin to become depressed, because the capacity to be depressed is a relatively mature experience, and in these patients represents a very real achievement.

I have seen this happen very gradually in a patient of poor prognosis, diagnosed, correctly I feel, as an hysterical psychopath. He was homosexual, delinquent, had attempted murder and had been in gaol more than once. For over ten years he has received supportive help during his recurrent crises, has gradually stabilized and is now following a creative career, though his crises continue. In the last twelve months I have watched him become depressed. He is only in this state for a few days at a time and it happens rarely, but when he is depressed he is assailed by guilt at the damage he has done in relationships, and shows a marked capacity for concern. In this state he is afraid of loss and abandonment, and this is an achievement, because it implies that he is at last able to aspire to an enduring relationship, and so loss has become a possibility. He now, at last, has something to lose, and he illustrates the fact that from the point of view of the "whole man" an individual may be much more healthy when he is in a state of depression than when he is not.

The proceedings of the symposia on depression held recently in Toronto and in Cambridge make interesting reading. They reveal a considerable controversy over such generally accepted beliefs as the efficacy of E.C.T. in endogenous depression. There is considerable doubt in the minds of some authorities as to whether E.C.T. actually is more effective in the long run than conservative management, and some believe that drugs such as Tofranil, when they work, do so by damping down symptoms without affecting the underlying depressive process. At the same time there is no agreement as to what the underlying depressive factor is. It seems, as one contributor aptly expressed it, that in psychiatry today our position is like what would have happened if half a dozen antibiotics had been introduced in the eighteenth century. The general view seems to have been that depression is a disease and that E.C.T. and Tofranil are highly effective in curing, at least temporarily, the more endogenous types of case. There were but one or two dissenters. These contributors pointed to the diminution of psychiatrists' tolerance of depression over the last fifteen years and to the role of E.C.T. in alleviating the psychiatrists' anxiety, that is, to its counter-transference significance. One pointed out that the psychiatrist might not be doing the patient a service by hurrying him along to E.C.T., but judging by the summary of the proceedings this opinion did not create much stir. These congressional proceedings illustrate how much it is taken for granted that depression, and not only depression of lethal severity, is an evil without meaning or purpose.

Continuing with the idea of growth as a process in which the conflicting parts of the individual come together, symptoms can often be seen as an expression of the struggle between the forces acting in the direction of bringing the parts together and those attempting to keep them separate. The "acting out" of conflicts in the external world is often an expression of this, and so at times is the request that a patient makes of a psychiatrist to help. It is an everyday experience to encounter the patient who arrives with a symptom, wanting it removed as soon as possible, and unable or unwilling to see any further significance in it. He wishes, as Glover has put it, to deposit his symptoms as a letter in a postbox disclaiming all further responsibility for it. If you decline to attack his symptom with vigour he may be hurt, puzzled or react more strongly. Let us say that his symptom refers to an unacknowledged hostility towards his wife whom he idealizes, and this idealization springs from unresolved difficulties in his relationship with his mother, who may be alive or dead. These contents, then, need to come to his consciousness and be resolved before the symptom will have done its work. On the other hand it may perhaps be a relatively simple matter to remove the symptom—a mild depression with amphetamine and reassurance, a travel phobia with barbiturates. Patient and doctor are extremely gratified and another cure is registered for that particular mode of therapy. The trouble about this, of course, is that neglected contents, like murder, will out, and the next time that the patient appears, be it in ten weeks or ten years, the problem may be more serious and less accessible. What will have happened in this case is that a part of the patient's personality has manipulated the doctor into doing its defensive work for it, to the detriment of the whole personality. This unconscious collusion between doctor and patient is probably very common indeed. In itself this is not necessarily a bad thing; it is sometimes justifiable or even advisable; but it is important that the doctor should know when it is going on. In other words, "defensive therapy" may be inevitable, but it should be conscious, at least in the psychiatrist's mind.

I have mentioned meeting the patient's needs, and by this I mean being prepared to listen to him, to hear the voices of his various divided parts, and to approach him not as a fragment but as a potential whole. As things stand in psychiatry today this is an almost impossible demand which can only be met for a proportion of patients in National Health practice. In private practice conditions tend to be more favourable and the difference between these two situations was summed up recently by a distinguished surgeon, who said that in N.H.S. practice the patient listens to the doctor, whilst in private practice the doctor listens to the patient. The greater the pressure of a waiting list, the more the initial interview becomes a matter of rapid diagnostic screening and the less the patient's needs are likely to be met.

So, in emphasizing Jung's concept of the self I do not imagine that what it implies in terms of the needs of the individual can be easily fulfilled. Despite this, psychiatrists could profit by it. I do not think that analysis is any panacea and regard as extremely limited its application to all cases of mental illness. On the other hand some neurotic disorders can only be resolved by the patient being allowed to regress within the security of the transference situation, and this is a process for which there are no short cuts. I would not regard a period of five years as long for this type of case but despite this regrettable limitation there does not seem to be any other way.

But however analysis may be limited in its application, the analytic attitude is not, and in a psychiatric Utopia the organically oriented psychiatrists will be as keenly interested in the unconscious as the analysts will be in the mode of action of drugs. The ideal out-patient N.H.S. psychiatrist will have trained his clerks, P.S.W.s and management committees so that he has the time, the capacity and the inclination to listen to his patients. He will be alive to the patient's unconscious processes and to the idea of the "whole man", and being flexible, he will not be deterred by having to make compromises frequently, but will be happy to pursue either physical or analytic therapy, depending on the case.

In contrast to this Utopian picture is one of a world in which nobody suffers any discomfort at all, because the doctors can relieve it at once. In this brave new world no one is grown up and there are no individuals. Lest this seem too extravagant let us remind ourselves of the glossy literature we get from the drug companies about the latest tranquillizers. They describe the power of their drugs to "normalize" the patient, as invaluable in the relief of unnecessary worry. The great potency and value of some of these drugs is now beyond dispute, but when they are used indiscriminately as symptom-eradicators without awareness of the dynamics and meaning of the underlying state the individuality of the patient has been forgotten. When this happens, the doctor is relating to a fragment and not to the patient as he really is, a potential whole.

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THE OCULAR MANIFESTATIONS OF CONGENITAL
TOXOPLASMOSIS IN FIVE OUT OF 686 CASES OF
MENTAL DEFICIENCY EXAMINED IN A STATE
INSTITUTION FOR MENTALLY RETARDED
CHILDREN, KINSTON, NORTH CAROLINA, U.S.A.

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TOXOPLASMOSIS is an infectious disease caused by a protozoal parasite of world-wide geographic distribution. The organism, *Toxoplasma gondii*, has been known since 1908, when it was demonstrated in the gundi, a North African rodent, by Nicolle and Manceaux and independently by Splendore in the rabbit in Brazil. Benda quotes Hellbrügge as mentioning that *Toxoplasma* apparently had been discovered in 1900 by Laveran, in the blood of a bird. It has since been found to be an infective agent in a great variety of species of rodents, mammals and birds from almost any part of the world, providing a large reservoir for human infection.

The rat, mouse, dog, hen, cow, goat, pig, sheep and many more display host susceptibility to the toxoplasma parasites, and serological evidence indicates that it has been responsible for infecting between 20 per cent. and 40 per cent. of the population in Britain (Beattie). The incidence of congenital toxoplasmosis in State Schools for Mental Defectives in the U.S.A. has been estimated at ranging from 0.2 per cent. to 0.05 per cent.

The first cases of proven human infection were detected in new-born infants by Wolf and Cowen in 1937. The parasite is crescentic-shaped, usually found in cells where it reproduces by fission. It shows a pronounced preference for chorio-retinal structures of the eye where it was observed by Wilder, Jacobs and others. Hogan was able to isolate the parasite from the eye of a case of congenital toxoplasmosis of twenty years' duration.

Aggregates of toxoplasma, often referred to as cysts, have been noted in sections of the brain, spinal cord, pancreas, lungs, liver, kidneys, suprarenals, gonads, myocardium and skeletal muscles. There the parasites may remain viable in the encysted stage for a long time, if not for the life of the host. The parasites are not infrequently released from the cyst walls, inducing a parasitaemia or localized inflammatory changes and scars in the uveal structures. This has been suggested to be the mechanism whereby recurrent attacks of human toxoplasmic chorio-retinitis are produced.

By means of the cytoplasm-modifying methylene-blue dye test developed

by Sabin-Feldman, complement-fixation test and toxoplasmin skin test, it has been demonstrated that patients with uveitis yield a higher proportion with immunological evidence of toxoplasmosis than is detectable in the general population. The fact that positive findings are recorded in the normal population, shows the widespread nature of this disease.

Toxoplasmosis, on the whole, does little harm in the adult population except in the acquired form which may be fatal. The human foetus, however, is particularly susceptible to the parasites which display a remarkable affinity for the central nervous system. The disease is transmitted at about the 5th month of pregnancy to the foetus through the placental circulation from a mother who has suffered from a recent infection. The disease, however, is usually subclinical and mild and rarely recognized. Such a mother may give birth to a child with signs of hydrocephaly, mental deficiency, microcephaly, epilepsy, chorio-retinitis, microphthalmia, optic atrophy and muscle paralysis. The mother usually develops immunity to the organism and rarely, if ever, has two children with the same disease. The new-born infant may show additional evidence of active infection by such signs as hepatomegaly, splenomegaly, icterus and a maculo-papular rash.

There has been much discussion about the level at which dye titres become of clinical significance. One sees, for example, children with convulsive disorders, or microcephaly or mental retardation without serologic evidence of toxoplasmosis, while all children and adults, with central chorio-retinitis significantly show high dye test antibody titres, whether or not other signs of congenital toxoplasmosis are present.

It is the opinion of Fair and others that the commonest clinical form of congenital toxoplasmosis is that in which only the uveal structures are involved. A varying degree of mental deficit is usually detectable. Patients with life-long central chorio-retinitis are frequently accompanied by positive skin tests and dye tests of rather low antibody titres, e.g. 1:32, 1:64 and 1:128.

These are the very titres reported in visually defective and blind patients who suffer from recurrent attacks of toxoplasmic chorio-retinitis unassociated with other clinical signs. Similarly, low titres were also observed in patients from whose blind eyes viable parasites were isolated (Jacobs). It is further held that the eye is capable of harbouring active toxoplasmic lesions without evoking high dye-test antibody titres or that the titres, after an initial rise, quickly fall to a moderate level. Low dye-test titres are thus quite specific for ocular toxoplasmosis, and a small active uveitis within one or both eyes may suffice to give rise to a moderate increase in serum antibodies.

A survey of 686 mental defectives, aged sixteen and under, and of patients with a history of long-standing visual handicap, was conducted at Caswell Training School, Kinston, North Carolina, U.S.A., in April, 1958. The team was composed of a consultant ophthalmologist and the writer, using the skin toxoplasmin test, dye-test and ophthalmoscopic techniques. Five mental defectives, four females and one male, were detected as showing the signs of the congenital form of toxoplasmosis with pronounced chorio-retinal manifestations.

Low dye-test titres and positive skin tests were obtained (Table I), and all patients had a history of defective vision of varying degrees; two patients had convulsive disorders of the major type and one showed intracranial calcifications of the diffuse, small circumscribed kind.

The five cases of congenital toxoplasmosis represent 0.7 per cent. of the 686 patients investigated and 0.25 per cent. of the total enrolment of 1930 patients resident at Caswell Training School.

TABLE I

Name	Case	Age	Sex	Skin Test		Dye Test	Skull X-rays
				Mothers	Patients		
Dorothy S.	.. 1	37	F	+	+	+1:32	Small circumscribed areas of calcification throughout.
Frances H.	.. 3	31	F	*	+	+1:128	No abnormal calcifications.
Mary C.	.. 2	18	F	+	+	+1:64	No abnormal calcifications.
Brenda C.	.. 4	12	F	+	+	+1:64	No abnormal calcifications.
Reginald G.	5	58	M	+	+	+1:64	No abnormal calcifications.

* Mother not available for skin test.

TABLE II

Name	No.	C.A.	I.Q.	Vision	Epilepsy	Grade
			(Binet)			
Dorothy S.	.. 1	37	48	Defective. Horizontal nystagmus internal squint (R.)	Major type	Mid-grade defective (imbecile)
Mary C.	.. 2	18	70	Defective. Left external squint	None	High-grade defective Familial type (F.M.)
Frances H.	.. 3	31	15	Almost blind in R. eye. Left eye removed	None	Low-grade defective microcephalic (Idiot)
Brenda C.	4	12	51	Very defective. Alternating internal squint	Major type	High-grade defective (F.M.)
Reginald G.	5	58	26	Grossly defective right cataract	None	Schizophrenia superimposed on mental deficiency, i.e. Pfitofschizophrenia

CASE REPORTS

Case I

Dorothy S., white, female, aged 37. History of grossly defective vision in both eyes. She is one of nine siblings (4th child); five are living and four dead. She is an epileptic of the major type. Father was an alcoholic and died of T.B. aged 33. Mother is still living and in good health. Parents were 2nd cousins. Patient had a record of backwardness at school.

Psychometric Test Data (Stanford-Binet):

26 January, 1928:	C.A. 6-11	M.A. 3-4	I.Q. 48
22 October, 1934:	C.A. 13-8	M.A. 6-8	I.Q. 49
5 March, 1953:	C.A. 32	M.A. 7-2	I.Q. 48

Fundoscopy examination discloses tremendous bilateral chorio-retinal scars in each macula. In the right fundus is a large healed scar, strongly pigmented. There is bilateral horizontal nystagmus and internal strabismus involving the right eye.

Skull X-ray shows "small circumscribed areas of calcification throughout cerebral structures".

Patient's Skin Test (Toxoplasmin): Strongly positive.

Mother's Skin Test (Toxoplasmin): Positive.

Dye-Test (drawn, April, 1958): Positive, 1:32 (result received 10 December, 1958).

Diagnosis: Confirmed case of congenital toxoplasmosis in a mid-grade defective female, with major epilepsy.

Case II

Mary C., white, female, aged 18, familial type. Youngest of 3 siblings; birth weight 5½ pounds. No childhood illnesses. Gait awkward and history of defective vision. Mother is a mental defective of high-grade level, and maternal grandfather was defective too. Whilst imprisoned for murder, he died of cardiac disease at the age of 73. Maternal grandmother was also a high-grade defective and in poor general health.

Psychological Test Data (Stanford-Binet):

8 February, 1952: C.A. 12-8 M.A. 8-10 I.Q. 70
Bellevue-Wechsler Scale for Children: V.I.Q. 65 P.I.Q. 68 F.I.Q. 63

Fundoscopic examination reveals bilateral chorio-retinal scars, heavily pigmented. Anterior segment clear in each eye. Left external squint.

Skull X-ray is essentially negative.

Patient's Skin Test (Toxoplasmin): Strongly positive.

Mother's Skin Test (Toxoplasmin): Positive.

Dye-Test (drawn, April, 1958): Positive, 1:64 (result received 10 December, 1958).

Diagnosis: Confirmed case of congenital toxoplasmosis in a high-grade mental defective female (familial type).

Case III

Frances H., white, female, aged 31. Full-term 6 pounds baby; labour uneventful. During first 3 months there were prolonged fits of crying. She commenced teething at one year and walking at three years with some difficulty. She has never talked. Her right eye was removed prior to admission to Caswell Training School (9 December, 1949). She is almost blind now, stunted in growth, poorly proportioned and microcephalic (cranial circumference 16¾ inches). Her older brother is normal. Parental history is not available.

Examination of left fundus shows large central chorio-retinitis. Microphthalmia left eye. Right eye surgically removed.

Skull X-rays: Essentially negative.

Patient's Skin Test (Toxoplasmin): Positive.

Mother's Skin Test (Toxoplasmin): Not available for test.

Dye-Test (drawn 1 April, 1958): Positive, 1:128 (result received 10 December, 1958).

Diagnosis: This is a confirmed case of congenital toxoplasmosis in a low-grade microcephalic mental defective female, associated with microphthalmia (L) and almost complete blindness.

Case IV

Brenda C., white, female, aged 12, second of seven siblings. Walking began at 18 months and talking at two years. She had whooping cough (1948), chicken pox (1948), measles (1952) and mumps (1953). Since her early childhood, she has had a record of major epileptic seizures. Father is in good health and of average intellectual ability. Mother is also normal.

Psychometric test (21 December, 1953) reveals C.A. 7-7, M.A. 3-10, I.Q. 51. Report adds that "patient shows extremely poor visual perception which cannot be improved with glasses".

Fundoscopic examination shows bilateral, central inactive chorio-retinitis. Each nerve head is quite pale but the vitreous body is clear. She also has alternating internal squint.

Skull X-rays: Essentially negative.

Patient's Skin Test (Toxoplasmin): Strongly positive.

Mother's Skin Test (Toxoplasmin): Positive.

Dye-Test (drawn 1 April, 1958): Positive 1:64 (result received 10 December, 1958).

Diagnosis: This is a confirmed case of toxoplasmosis in a high-grade defective female, with major epilepsy.

Case V

Reginald G., white, male, aged 58. He was considered mentally defective by his family but no detailed information is available regarding his developmental data except that he commenced walking at 2 years 3 months. He often expressed ideas that someone was out to harm him. He threatened on several occasions to commit suicide, and once he caught the coloured maid by the throat threatening to kill her. He gradually deteriorated, becoming temperamentally unstable and unmanageable. He is said to have set fire to a barn belonging to his parents when he was an adolescent. His father was a severe diabetic and the mother, who is still living, is in good health and mentally normal; a maternal aunt, however, was an epileptic suffering from major seizures.

Psychometric Test reveals (20 July, 1945) a C.A. 44-11, M.A. 2-6, and an I.Q. of 20, on the Kuhlmann Infant Scale. The psychologist further states "that the patient belongs to the

group of persons generally referred to as pseudo-mentally retarded, in view of his long history of delusions and hallucinations which are superimposed on a basic mental backwardness. In April, 1953, the patient's test data were C.A. 52-7, M.A. 4-1, I.Q. 26. The increase in the test score over the one obtained in 1945, is apparently an indication of a lessening of the intensity of the psychogenic disorder (Pfpopschizophrenia)".

Fundoscopic examination of right fundus "shows advanced cortical and nuclear cataract with no sign of old inflammation externally. The left lens is clear. There are a few small floating exudates in the vitreous humour and a large central chorio-retinal scar".

Skull X-rays "are essentially negative".

Patient's Skin Test (Toxoplasmin): Strongly positive.

Mother's Skin Test (Toxoplasmin): Positive.

Dye-test (drawn 1 April, 1958): Positive, 1:64 (result received 10 December, 1958).

Diagnosis: This is a confirmed case of congenital toxoplasmosis in a mid-grade mental defective male with superimposed schizophrenic psychosis described as Pfpopschizophrenia.

SUMMARY

In a survey of 686 mental defectives, undertaken in April, 1958, by a consultant ophthalmologist and the writer at Caswell Training School, Kinston, N.C., comprising a total enrolment of 1,930 residents at the time of the study, five patients, four females and one male, were diagnosed as showing the clinical signs of congenital toxoplasmosis. Four patients had I.Q.s ranging from 15 to 70 points and one, being a case of chronic schizophrenia superimposed upon a condition of mental deficiency (Pfpopschizophrenia), an I.Q. of 26 points.

Intracranial calcifications were radiologically demonstrable in one patient (No. 1), and a history of major convulsions was recorded in cases No. 1 and No. 4. A history of visual handicap was reported in all patients, and a condition of cataract in the right eye was seen in case No. 5.

The skin toxoplasmin tests were positive in all of the five mental defectives and also in four of the patients' mothers; one mother, however, was not available for the skin test. The Sabin-Feldman methylene-blue dye test was positive in all patients, showing antibody titres ranging from 1:32, 1:64, to 1:128.

These low antibody titres were probably indicative of the large but localized toxoplasmodic lesions affecting the uveal structures primarily and to a lesser extent the smaller but more diffusely placed lesions in the central nervous and visceral systems.

In conclusion one may state that congenital toxoplasmosis is an important aetiological factor in the production of central, bilateral chorio-retinal lesions, and often the only clinical sign seen of the disease; it is also a pre-natal agency in the causation of mental deficiency of varying degrees and of developmental anomalies.

In addition one is right in saying that a mother, having borne one affected infant, develops such a degree of active immunity to toxoplasmosis that there is little risk of her bearing a second child similarly affected. Owing to the wide-spread distribution and frequency of toxoplasmosis in the normal population, attempts will have to be made to immunize previously uninfected pregnant mothers, in order to reduce the incidence of foetal infection and its undesirable consequences.

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A REPORT ON THE EFFECTS OF PHENELZINE (NARDIL), A MONOAMINE OXIDASE INHIBITOR, IN DEPRESSED PATIENTS

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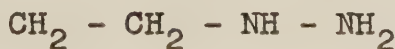
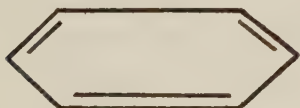
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INTRODUCTION

PHENELZINE, β -phenylethylhydrazine, of structural formula, is regarded as a



potent, rapidly acting, long-lasting monoamine oxidase (M.A.O.) inhibitor. The administration of such compounds protects 5-hydroxytryptamine (serotonin) which is destroyed by M.A.O. 5-hydroxytryptamine is believed to act in the brain as a chemical mediator, the function of which is to control the pulsating action of oligodendroglial cells which supply the other brain tissues with nutrient. It has been suggested that a relative 5-hydroxytryptamine deficiency is the fundamental biochemical disorder of severe depressive states and that M.A.O. inhibitors such as phenelzine tend to promote restoration to more normal concentration and activity.

However, a recent leading article (1) comments on observations which make it difficult to relate the central action of M.A.O. inhibitors to an effect on the rate of inactivation of the catechol amines.

Phenelzine is said to exhibit adequate anti-depressant activity at dosage levels that are without serious toxicity. Claims are made for an effect comparable in scope, speed and safety to that produced by electro-convulsive therapy.

All published reports of clinical trials known to the authors have come from the United States in the last year or so and in the treatment of endogenous depression they generally accept that phenelzine is active.

For example Thal (2) in comparing the usefulness of eleven anti-depressant drugs found phenelzine to be the most valuable tested. He noted that relief in some patients commenced within 4–8 hours. Recovery was usually noted in 2 or 3 weeks and was maintained after discontinuation of the medication. Haematological, blood chemistry and liver function tests carried out at weekly intervals before, during and after treatment were found to be normal.

Furst (3) treated a group of 50 out-patients from private practice with severe depressive illness. Dosage varied from 60–90 mg. daily in divided doses. If response occurred within one week or less, the dosage was gradually reduced. A maintenance level was eventually achieved in about 4 weeks and was continued for a further 2–3 months. Side-effects were minimal. Complete remissions were observed in 69 per cent. of the patients.

Arnow (4) analysed 580 case records from 16 investigations and reported that the great majority of patients with endogenous depressions respond favourably to phenelzine and only a small minority need E.C.T. He comments that freedom from clinically important side-effects and the specificity of the drug allow its use as a diagnostic measure.

In this country Hutchinson and Smedberg (7) have reported the results of a double-blind crossover trial as follows: "34 depressed female in-patients who had failed to respond to other treatment. Nine (26 per cent.) patients were discharged, 13 (30 per cent.) showed great improvement and 14 (41 per cent.) were regarded as moderately or slightly improved. Five patients (14 per cent.) were made worse." He considers that phenelzine has a place in the treatment of depression and comments on the absence of side-effects.

METHOD

A pilot double-blind study preceded an ordinary clinical trial.

Subjects totalling 68 men and 64 women (of whom 14 per cent. were aged 18 to 30, 66 per cent. 31 to 60, and 20 per cent. 61 or over) were either in-patients or attending at a Day Hospital. The majority were suffering from obvious endogenous depression of a moderate to severe degree. The preliminary and subsequent weekly assessments were made on the basis of the following symptom rating scale:

- I. Morbid thoughts and feelings; e.g. ideas of reference, suicidal ideas, ideas of unworthiness, somatic delusions, obsessions, etc.
- II. Feelings of depression.
- III. Loss of interest, fatigue, lack of energy.
- IV. Agitation (including restlessness, irritability and tension).
- V. Sleep disturbance.
- VI. Disturbance of appetite and loss of weight.

Scoring: 0=not present; A=mild; B=moderate; C=severe.

The double-blind trial, in which placebo and active agent were each given for a fortnight, conformed to an accepted pattern in which the order of administration was only known to the dispenser.

The maker's recommended dosage of three 15 mg. tablets daily was used throughout in this part of the study.

For the rest there was some variation according to accumulating clinical experience. The commencing dose of 3 or 4 tablets daily was increased if necessary by 1 tablet daily at weekly intervals. No patient received more than 6 tablets daily.

Final results of treatment were rated as follows: fully recovered, much improved, improved, no change or worse.

RESULTS

I. DOUBLE BLIND TRIAL

(a) *Placebo 1st fortnight* (17 patients)

Statistical comparisons

Pre-treatment rating with 2nd placebo week no significant difference.

Pre-treatment rating with last week (2nd week on active agent) significant at $< .01$ level of confidence.

Second placebo week with 2nd week on active agent significant at $< .01$ level.

(b) *Active agent 1st fortnight* (8 patients)

Comparisons of weekly ratings did not show any significant degree of difference. However, this small group of patients had a proportionately greater share of the failures (5 out of 8).

It seemed reasonable to assume that beneficial effects of the active agent accounted for the results in (a) above thus justifying the commencement of an ordinary more extensive clinical trial of the drug.

Below is an analysis of the results in a group of 132 patients (68 male and 64 female) who had the drug for 2 weeks or more.

II. ORDINARY CLINICAL TRIAL

(a) *Males* (68)

Recovered	29.4%	} 52.9%	} 63.2%
Much improved	23.5%		
Improved	10.3%		
No change or worse	36.5%		

χ^2 not significant at .05/.01 unless "recovered" and "much improved" groups are taken together.

(b) *Females* (64)

Recovered	47.0%	} 59.5%	} 70.4%	
Much improved	12.5%			
Improved	10.9%			
No change or worse	29.6%			
χ^2 highly significant	< .01			

DIAGNOSTIC CATEGORIES

Males:

First depression (33)	$\chi^2=19.6$
(significant at .01 level)	
Recurrent depression .. (12)	$\chi^2=1.97$
(not significant)	
Involucional depression .. (4)	$\chi^2=0$
(not significant)	
Senile (8)	$\chi^2=1.0$
(not significant)	
Reactive	} .. (11) (too small for χ^2)
Psychoneurotic states	
Schizo-affective states	

Females:

First depression (11)	$\chi^2=5.08$
(nearly significant at .05 level	
(.05=5.99))	
Recurrent depression (22)	$\chi^2=14.6$
(significant at .01 level)	
Involucional/menopausal depression (15)	$\chi^2=12.9$
(significant at .01 level)	
Senile (6)	$\chi^2=.16$
(not significant)	
Reactive depression (7)	$\chi^2=2.83$
(not significant)	
Schizo-affective states (3)	(too small for χ^2)

Note i: The group of first depressions excluded those patients falling ill for the first time in the involucional or senile periods.

Note ii: The numbers of "recovered" and "much improved" patients were taken together in this analysis of diagnostic categories.

SIDE-EFFECTS

In at least one-third of the women but in only a small number of the men there were complaints of dizziness, unsteadiness and drunken feelings, particularly in the first few days, and more so in those patients, mainly women, receiving higher dosage. One patient receiving 6 tablets daily was confined to bed for several days with marked postural hypotension (B.P. supine 140/95 to 110/80 compared with 75/45 to 65/35 after 5 minutes standing). Tolerance quickly developed, and if not, beneficial effects of the drug were compensatory. Some distinguished between active agent and placebo because of the absence of dizziness with the latter tablets, thus confirming a genuine side-effect.

In 15 women and one man oedema of the feet, ankles and legs of varying degrees of severity occurred usually after no less than 2 weeks at high dosages (4-6 tablets a day). However, 2 patients on the recommended dosage of 3 tablets a day are included. In 3 women the oedema seemed more generalized involving the hands and face. It is of interest that 13 out of 16 patients with oedema responded well to treatment as regards their psychiatric symptoms. Without exception oedema cleared up when medication ceased or dosage was reduced to a minimum.

Difficulty in starting micturition was noted in the cases of 2 men and 3 women when dosages were increased. A critical level between 3 and 4 tablets a day was demonstrated for one patient. Once again tolerance developed quite quickly.

Two men and 3 women became mildly hypomanic on phenelzine. In only 2 was there definite evidence of previous mood swings in this direction.

Several women developed a craving for chocolates and sweets which seemed related to effects of the drug. There was quite a dramatic increase in weight in two of these patients (2 stones in 2-3 months).

One patient on 6 tablets a day for many weeks who showed generalized oedema, developed a vertigo which has remitted since treatment ceased.

The significance of complaints about constipation is not easy to assess.

Our experience does not support claims for minimal or complete freedom from side-effects. However, whilst the incidence is relatively high these are not severe and can be easily reversed. There has been no clinical evidence of toxic damage such as disorder of the haemopoietic system, kidneys or liver function, although Kathari (5) reports that 7 out of 13 cases showed some abnormality in liver function tests on 15 mg. of phenelzine t.i.d. Findings which contrast with those of Furst (3). His pre-test analysis, C.B.C., alkaline phosphatase, thymol turbidity and cephalin flocculation tests on 30 cases did not differ significantly with those taken after the second month of ingestion.

Our routine investigation in cases with oedema has not provided any data pointing to its cause.

Five patients have had EEG recordings before and after treatment. No significant changes have been observed such as are comparable with those due to E.C.T.

We have commented (6) previously on the absence of side-effects when E.C.T. is given with or immediately following a course of phenelzine.

Because of a tendency to relapse on withdrawal of the drug it was found possible to keep several women in the involutional group on high dosage, e.g. 4-5 tablets a day for as much as 3-5 months followed in a few cases by a maintenance dose of 1-2 tablets a day.

DISCUSSION AND CONCLUSIONS

Our findings support the claims for the usefulness of phenelzine in typical endogenous depressions.

In the 6 schizo-affective states characterized by depressive feelings and relatively milder forms of thought disorders (e.g. only one patient had hallucinations) there were no beneficial effects at all.

Only one out of 6 patients who seemed to have depression secondary to a psychoneurosis showed any benefit.

The better results on the female side may well represent a true sex difference but further confirmation is needed, paying particular regard to the involutional/menopausal category which showed the best response of all.

We were not clinically impressed by the effects in the senile and reactive groups although numbers involved are too small for a firm appraisal.

Patients with marked agitation did not benefit and in some cases were thought to be made worse.

Of 21 patients who failed to respond to phenelzine and subsequently had E.C.T., 10 did well. Only 3 patients with recurrent depressions, who had previously benefited from E.C.T., did not improve on phenelzine. We feel

that had all patients been given E.C.T. the initial results would have been better by between 5 and 10 per cent.

No follow up study of the relapse rates has yet been attempted. However, our experience to date leads us to assume that the relapse rate in the first few weeks after the drug is discontinued is perhaps less than we would have anticipated had E.C.T. been the treatment. Duration of treatment in patients who have responded has varied from 1 to more than 6 months (including maintenance dosage).

Relapses whilst on maintenance dosage have again responded to increased dosage. In a group of 20 females given placebo at the third week those responding, but still with symptoms, showed mild to quite marked relapses after the first few days with a quick reversal on returning to active agent.

Ten patients who failed to respond to phenelzine were then given Tofranil and only 2 seemed to benefit.

Earlier observations in the fairly rapid action of phenelzine are confirmed. Significant responses have been seen within 24 hours and for the majority before the second week. Such features are of considerable importance if this drug is going to be used at large, where perhaps morbidity risks will not be so carefully assessed. Suicidal thoughts need not by any means always call for hospitalization and E.C.T. However, in treating such patients with the newer anti-depressants the general practitioner should consider daily assessments until he is certain of a response or of failure.

SUMMARY

A controlled trial was carried out to evaluate the effects of phenelzine on mainly endogenous types of depressive illness. The results are regarded as largely validating the claims for the drug's therapeutic value, and that it has an effect comparable in scope, speed and safety to that produced by E.C.T.

In a preliminary double-blind study a comparison of symptom rating when 2 weeks of placebo were followed by 2 weeks of active agent showed a significant difference at the $\cdot 01$ level of confidence.

In the routine clinical trial which followed the results with female patients were highly significant ($< \cdot 01$).

The males did less well in this study and results in terms of χ^2 achieve the $\cdot 05/\cdot 01$ level of confidence only when the totals of recovered and much improved patients are taken together.

70.1 per cent. of the females and 63.2 per cent. of the males showed some response to treatment.

True but easily reversible side-effects have been noted including dizziness, oedema—mainly of the lower limbs, difficulty of micturition and hypomania.

ACKNOWLEDGMENTS

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PSYCHIATRIC ILLNESS AND PERNICIOUS ANAEMIA: A CLINICAL RE-EVALUATION

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INTRODUCTION

ADDISON (1855) in his classical description wrote of the patient's mind "as occasionally wandering" during the final stages of pernicious anaemia. The relative frequency with which different psychiatric syndromes present differs from that recorded by previous writers and is probably due to earlier psychiatric consultation in the present group, though mode of referral may also play a part. Bowman (1935) found organic confusion in 48 per cent., a death rate of 35 per cent. and a red blood cell count of below 4·0 million in 65 per cent. of his 23 cases. Herman, Most and Joliffe (1937) found organic confusion in 35 per cent. compared with the present writer's 5 per cent., a death rate of 22·5 per cent. compared with 10 per cent. and a red blood cell count of under 3·0 million in 75 per cent. of his 40 cases, compared with 25 per cent. of the present group.

The present author, having recently had experience of several patients suffering with both psychiatric illness and pernicious anaemia, obtained access to the records of 20 patients admitted to the Bethlem Royal and Maudsley Hospitals with this combined diagnosis and re-evaluated the clinical records in an attempt to define more precisely the relationship. The 20 patients had been admitted during the years 1948-1959 and represent 0·1 per cent. of the total number of psychiatric patients aged 35 years or over seen during this period.

The literature reveals that the association of pernicious anaemia and psychiatric illness is too often interpreted as implying a major causal relationship. With the acceptance of multiple causation in the production of psychiatric reactions, only a detailed analysis of case material can allow judgments to be made regarding the relative importance of pernicious anaemia, compared with other factors in the aetiology of psychiatric illness. The aetiological importance of pernicious anaemia in the psychiatric illnesses presented in this paper can be accepted if there are not other equally or more satisfactory factors contributory to the mental state or if the mental state is specific. The latter does not appear to be the case though paranoid symptoms are regarded as being present in a high proportion of patients and 65 per cent. of the present series had paranoid symptoms. The natural history of the psychiatric disorder, the environmental changes resulting from hospital admission and the physical conditions associated with old age are some of the factors requiring assessment in order to evaluate the psychiatric state and course, before assuming the aetiological importance of vitamin B₁₂ deficiency in the psychiatric illness.

At our present state of knowledge, the author considers it wiser to establish strict criteria before accepting the aetiological importance of pernicious anaemia in psychiatric illness and they should ideally be (1) no past history of

psychiatric illness; (2) no evidence of disturbed pre-morbid personality; (3) absence of psychologically or socially disturbing events preceding the illness; (4) unequivocal presence of a mental illness; (5) associated and proven pernicious anaemia; (6) resolution of a mental illness with vitamin B₁₂ treatment; (7) relapse when vitamin B₁₂ is withheld; (8) neuropathological evidence of vitamin B₁₂ deficiency.

The case reports presented as an appendix are briefly analysed in an attempt to approach the theoretical viewpoint outlined in the preceding paragraph.

CLINICAL DATA

Pernicious anaemia was diagnosed on the basis of clinical history and examination, coupled with full blood count, histamine-fast achlorhydria and/or megaloblastic bone marrow in 17 patients. In 3 patients only a blood count and film was done. Table I, below, summarizes the data on psychiatric diagnosis, age, neurological state and blood count.

TABLE I

Case No.	Sex	Diagnosis	Age in Years	Neurological Abnormality	At Time of Psychiatric Presentation		
					Hb%	R.B.C. 10 ⁶ /cu.μ	M.C.V. 78-94 cu.μ
1	F	Dementia	73	Present	96	3.9	—
2	F	Senile paranoid state ..	76	Present	83	4.5	—
3	*F	Depression	66	Present	90	4.0	90
4	*F	Hysteria	48	Present	52	2.8	89
5	F	Dementia	70	—	109	5.2	100
6	F	Senile paranoid state ..	70	—	96	4.5	102
7	*F	Depression	79	—	63	3.5	105
8	F	Hypomania	57	—	86	4.7	—
9	F	Dementia	68	—	94	4.7	95
10	*F	Depression	64	—	54	2.7	111
11	*F	Hysteria	47	Present	88	3.6	117
12	M	Dementia	64	Present	86	4.8	91
13	*M	Dementia	84	Present	30	—	—
14	*M	Depression	42	Present	47	2.0	118
15	*M	(a) Acute confusion ..	38	Present	56	2.4	102
		(b) Schizo-affective state	42	Present			
16	*M	Depression	75	—	52	2.2	104
17	*M	Depression	64	Present	60	1.6	—
18	M	Depression	62	Present	75	3.2	125
19	M	Alcoholic hallucinosis ..	46	Present	84	4.2	105
20	M	Depression	62	Present	90	4.8	96

Asterisks denote those patients who presented psychiatrically and a diagnosis was made by the psychiatrist.

The average age at the time of psychiatric presentation was 64.7 years with a range of 38 years–84 years. The average length of psychiatric history was 12.4 months with a range of 2 weeks–7 years. From these figures, the average length of time between the diagnosis of pernicious anaemia and the onset of the psychiatric disorder was calculated as 3.0 years.

The functional psychoses diagnosed in 12 patients consisted of 8 patients with depressive illness, 1 with hypomania, 1 with a schizo-affective state and 2 with senile paranoid states. The 7 organic states consisted of 1 acute confusional state, 1 alcoholic hallucinosis and 5 dementias. The neuroses were represented by 2 patients with conversion hysteria. No attempt was made to assess personality though it seems worth recording that half of the group were described as “methodical”, “conscientious”, “hardworking”, or “responsible” in their occupation.

Table II, summarizes data on physical state, treatment and outcome.

TABLE II

Case No.	Age in Years	Diagnosis	Physical Abnormality	*Specific Treatment	Improvement 0-4 Plus
1	73	Dementia	Arteriosclerotic heart failure	E.C.T.	++
2	76	Senile paranoid state	Bilateral cataracts, osteoporosis of spine	—	0
3	66	Depression	Bilateral cataracts	—	+++
4	48	Hysteria	—	—	+
5	70	Dementia	Arteriosclerotic heart disease	—	0
6	70	Senile paranoid state	Gross arteriosclerosis	—	0
7	79	Depression	—	—	0
8	57	Hypomania	—	—	++++
9	68	Dementia	Arteriosclerosis with hypertension	E.C.T.	++
10	64	Depression	Rheumatoid arthritis, varicose ulcers of legs	E.C.T.	++++
11	47	Hysteria	Disseminated sclerosis	—	+
12	64	Dementia	Bilateral cataracts	Phenelzine	+
13	84	Dementia	—	Phenelzine	+
14	42	Depression	—	—	++++
15	38	(a) Acute confusion	—	—	++++
	42	(b) Schizo-affective state	—	—	++++
16	75	Depression	Arteriosclerosis	E.C.T.	+++
17	64	Depression	Gout	—	++++
18	62	Depression	—	—	++++
19	46	Alcoholic hallucinosis	—	—	++++
20	62	Depression	Hypertension	—	+++

* Denotes treatment other than vitamin B₁₂ or general in-patient routine. Cases Nos. 1-11 are females, Nos. 12-20 are males.

A diagnosis of dementia was made in Cases Nos. 1, 5, 9, 12 and 13. Of this group Cases Nos. 1, 5 and 9 had evidence of gross cardiovascular disease, were over 65 years of age, had satisfactory blood counts and failed to respond to vitamin B₁₂ treatment. The neurological abnormalities sufficient to warrant a clinical diagnosis of vitamin B₁₂ neuropathy (Jewsbury, 1954) in Case No. 1 was not supported by post-mortem examination and exemplifies the difficulty in assessing the pathological significance of neurological abnormality in old age (Critchley, 1931). In Case No. 1 pernicious anaemia presented with acute confusional state 8 years prior to the dementia and in Case No. 9 a severe physical illness 6 months prior to psychiatric presentation. Thus, though pernicious anaemia may be considered contributory to the psychiatric illness, particularly in Case No. 9, the factors described above that are common to the 3 cases appear to be of greater aetiological significance. Case No. 12 had cortical atrophy, episodic loss of consciousness, normal serum B₁₂ levels, and failed to respond to vitamin B₁₂ treatment suggesting a dementia of primary origin, rather than secondary to vitamin B₁₂ deficiency. The EEG changes suggest the latter and a prolonged follow-up will be necessary to clarify the diagnosis. In Case No. 13 an old man of 84 years, there was insufficient information to reach a conclusion.

Cases Nos. 2 and 6 were both 70 years or over, the former had senile changes in her spine and eyes, the latter gross arteriosclerosis. Both had siblings with a history of psychiatric illness and both patients failed to respond to vitamin B₁₂ treatment. Thus senile cerebral changes in genetically predisposed individuals

seems a more satisfactory formulation of their psychiatric illness than pernicious anaemia.

Of the patients with affective disorders, Cases Nos. 3 and 20 showed slow resolution of their depressive illness with general supportive measures following hospital admission. As Case No. 20 had an 8-year history of pernicious anaemia, a spontaneous recovery of his depression seems the likeliest explanation and though less likely an explanation in Case No. 3 this cannot be excluded. Cases Nos. 10 and 16 failed to respond to vitamin B₁₂ treatment but responded to E.C.T. suggesting that the depressive illness was independent of pernicious anaemia. The depression in Case No. 17 resolved prior to the diagnosis of pernicious anaemia being made, his hospital admission resulting in separation from a demanding fiancée. Case No. 17 is thus an example of Engyesis (Davies, 1956). Case No. 18, a patient with manic depressive psychosis, stayed too short a time in hospital for adequate assessment.

Cases Nos. 4 and 11 had a long history of hysterical symptoms on a basis of personality disorder and responded little to vitamin B₁₂ treatment, whilst Case No. 19 repeated his past pattern of response to 2 weeks abstinence from alcohol.

Of the remainder, Case No. 15 presented with symptoms of an acute confusional state which responded dramatically to vitamin B₁₂ treatment whilst equal therapeutic success was seen in Cases Nos. 7, 14 and 18. Case No. 7 who had a past history of depressive illness 10 years previously appeared to react adversely to disagreements with her son but though the external situation did not change, she lost her morbid ideas and was able to deal realistically with the situation, within 10 days of commencing vitamin B₁₂ treatment. Case No. 14, who had failed to respond to orthodox treatment for his depression, responded rapidly to vitamin B₁₂ treatment once the correct diagnosis was established and he made a complete recovery. Case No. 18 showed a therapeutic response on 2 occasions to vitamin B₁₂ treatment once the diagnosis of pernicious anaemia was made, the last illness resolving within three weeks.

No relationship between psychiatric improvement and change in blood count or neurological state was found, only 1 case showing improvement of the latter with psychiatric improvement. Also no relationship was found between the severity of the psychiatric illness, e.g. degree of depression and the neurological state.

DISCUSSION

It is thus apparent that if an attempt is made to apply the 8 criteria proposed in the introduction of 20 patients, only 4 cases (Cases Nos. 7, 14, 15 and 18) might be considered examples of psychiatric illness secondary to pernicious anaemia, the evidence being most convincing in Case No. 14 and 15(a). In an attempt to find external validation for this view the author reviews below studies relevant to the possible underlying mechanisms for understanding this relationship and indicates which aspects support the clinical analysis above.

Following the discovery of abnormal electro-encephalograms in patients with pernicious anaemia (Romano and Engel, 1944), Samson, Swisher, Christian and Engel (1952), studied 14 patients with pernicious anaemia by serial EEGs. A delirious state was diagnosed in 13 patients, though the criteria for this diagnosis would not necessarily be generally accepted and 12 patients suffered with sub-acute combined degeneration. A qualitative frequency analysis of the

EEG carried out on 11 patients revealed that 9 showed significant EEG improvement during vitamin B₁₂ treatment, 6 having a return to a normal EEG pattern. It is of particular interest that the EEG improvement preceded any change in red blood cell count though it approximated to the time of the reticulocyte response. Walton, Kilott, Osselton and Farrall (1954) studied the EEG of 80 patients with pernicious anaemia in relapse, 50 under treatment and 10 patients with miscellaneous anaemia. Of 80 patients, 64 per cent. had abnormal EEGs which bore no relationship to age, degree of anaemia or presence of neurological involvement. Those patients showing sub-acute delirious reactions had abnormal EEG records which reverted to normal within 7-10 days following the commencement of treatment. However, despite this, there was not a close relationship between EEG abnormality and mental state.

Scheinberg (1951) basing his technique on the nitrous oxide method of Kety and Schmidt, studied the cerebral metabolism of 16 patients with pernicious anaemia. Fifteen of the group had sub-acute combined degeneration and 13 were in haematological relapse. The abnormal mental status was briefly recorded from 1 plus to 4 plus on the presence of organic mental symptoms, 15 patients being classified. EEGs were performed on 11 out of 16 patients. Scheinberg found a good correlation between severe neurological involvement, abnormal mental status and low cerebral oxygen consumption and that cerebral metabolism reverted towards normal with vitamin B₁₂ treatment though not completely so.

It is not possible at the present time to specify precisely the biochemical functions of vitamin B₁₂ either within the central nervous systems or the body generally. Nevertheless, certain reactions pertaining to the function of the former have been described. Ling and Chow (1953) demonstrated an increase to normal in blood sulphydral compounds (mainly the glutathione fraction) in 2 pernicious anaemia patients following vitamin B₁₂ treatment. Glutathione is probably a co-enzyme in one of the steps of glucose metabolism (Strickland, 1956) and glucose is the main source of energy for the brain. In this respect it is of interest to note that Earl, Hawary, Thompson and Webster (1953) demonstrated an abnormal pyruvate curve in 3 cases of untreated sub-acute combined degeneration, the curve returning to normal with vitamin B₁₂ treatment. The phospholipids, lecithin and kephalin found in great abundance in the white matter of brain contain modified forms of serine and the latter's conversion from glycine requires the presence of vitamin B₁₂ (Bicknell and Prescott, 1953). Nucleic acid and its nucleotide subgroups are essential constituents of nerve cell cytoplasm and nuclei, and ribose nucleic acid (R.N.A.) is found to disappear from the cytoplasm on electrical stimulation of nerves (Canterow and Schepartz, 1954). Vitamin B₁₂ is involved in nucleic acid synthesis and is required for the formation of deoxyribose nucleic acid *via* thymidine synthesis. Vitamin B₁₂ may thus be seen to play an essential part in chemical reactions relating to carbohydrate metabolism, phospholipid and nucleic acid formation, all of major importance to the central nervous system. A summary of recent research is available from the proceedings of the 4th International Congress of Biochemistry (Arnstein, 1960).

The four cases (Nos. 7, 14, 15 and 18) presented above illustrate some aspects of the above findings. Thus clinical response was marked within 3 weeks and this parallels the cerebral physiological disturbance noted in the EEG and metabolic studies presented above, in which reversion to normal occurred 7-10 days following the commencement of vitamin B₁₂ treatment. The cases also agree with the EEG studies in failing to find correlation between blood

count, neurological status and improvement. Thus Case No. 15 (first admission) showed a fall in haemoglobin level in the presence of marked psychiatric improvement following vitamin B₁₂ treatment. Though the possible biochemical disturbance underlying the physiological ones are briefly sketched insufficient detailed knowledge of the chemical reactions precludes further worthwhile discussion of this relationship.

The availability of radioactive isotopes of vitamin B₁₂ provides a useful tool for studying the relationship of pernicious anaemia and psychiatric illness. However, unless the clinician can define more clearly the syndromes he meets in practice, inconclusive results will inevitably follow the application of precise techniques to a heterogeneous sample of patients.

SUMMARY

Twenty patients with psychiatric illness and pernicious anaemia have been clinically re-evaluated with particular emphasis on their aetiological relationship. It is argued that only 20 per cent. of cases falling into this group show a direct relationship between their psychiatric illness and pernicious anaemia. Pertinent studies of cerebral metabolism to support the view presented in this paper are reviewed.

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APPENDIX

BRIEF CLINICAL SUMMARY OF CASES

Case No. 1

Mrs. F.P., aged 73 years. Family history of 1 brother "neurasthenic" and 1 sister who died in a mental hospital. Past history of puerperal depression at the age of 25 years and certified at the age of 65 years with a diagnosis of "acute confusional state". Recovery followed treatment with "Anahaemin" after pernicious anaemia was diagnosed at a general hospital.

Present history (of two months duration), of fatigue, dyspnoea and wandering, incoherent talk, delusions of being poisoned, disorientation, depression and incontinence.

Physical examination: B.P. 170/100, enlarged left cardiac ventricle, absent ankle reflexes and Rhombergism present. A Hb. was 96 per cent., R.B.C. was 3.9 million, W.C.C. was 5,500 c.mm. and blood films showed slight macrocytosis. "Campolon" and "Cytamen" were given, followed by 3 E.C.T.s because of persistent marked depression. The depression resolved and the dementia became more marked. Re-admitted 1 year later, depressed negativistic and

disorientated. Hb. was 89 per cent. and R.B.C. was 4.0 million. Death occurred 1 year later from heart failure. Post-mortem revealed senile dementia, arteriosclerotic left ventricular failure, but no evidence of subacute combined degeneration.

Case No. 2

Miss M.B., aged 76 years. Diagnosed pernicious anaemia 11 years previously. Family history of 1 sister aged 40 years with affective disorder.

Present history of 1 month's duration, ideas of reference, delusions of being poisoned, that she can perform miracles.

Physical examination revealed cataract of both eyes, absent knee and ankle reflexes and senile osteoporosis of the spine. A Hb. of 83 per cent., R.B.C. of 4.5 million and W.C.C. of 9,500 c.mm. was reported. No change in her clinical state was noted on discharge after 4 months treatment with "Anahaemin".

Case No. 3

Mrs. G.C., aged 66 years.

Present history of 6 months duration of leg pains, tiredness and depression preceded by deteriorating vision and housing problems. Examination revealed bilateral cataracts, a bromide rash with mild confusion which resolved within 2 weeks revealing an underlying agitated depression; weakness and spasticity of both legs, diminished vibration sense and unequal ankle reflexes were present. Hb. was 90 per cent., R.B.C. was 4.0 million and W.C.C. was 8,600. "Camplon" was prescribed daily and the mental state slowly resolved over the next 3 months with no change in blood picture or neurological state.

Case No. 4

Mrs. L.E., aged 48 years.

Past history of nail biting and somnambulism as a child and sexual frigidity in adulthood. At the age of 31 years she developed hysterical paralysis of legs following her father's death.

Present history of 1 month's inability to walk, hysterical amnesia and depression within 8 weeks of a pan-hysterectomy. Examination revealed loss of postural sense in legs, absent ankle and knee reflexes, parasthesiae in fingers and toes, with hysterical anaesthesia of the legs. Hb. was 52 per cent., R.B.C. was 2.8 million, W.C.C. was 6,400 c.mm. and blood film was macrocytic. Massive "Cytamen" dosage was given and 5 months later she had a Hb. of 80 per cent. and R.B.C. of 4.2 million. On discharge 2 years following admission her Hb. was 95 per cent., R.B.C. was 5.0 million, her gait had greatly improved, the reflexes were still absent with absence of vibration and postural sense in legs. Psychiatrically she showed variable depression, emotional instability and occasional vomiting, but no amnesia.

Case No. 5

Miss R. G., aged 70 years.

Present history of 1 month's confusion wandering and talking to herself. On examination she misidentified people, she showed lability of mood, amnesia, disorientation, incontinence and delusions of being poisoned. Physically, the patient had slurred speech, tremor of arms, hyperaesthesiae of both feet, enlarged heart and auricular fibrillation. The E.C.G. supported a diagnosis of degenerative heart disease. Hb. was 109 per cent., R.B.C. was 5.2 million and W.C.C. was 9,000 c.mm. "Cytamen" was given with little clinical change.

Case No. 6

Mrs. A.L., aged 70 years. Family history of schizophrenia affecting 1 brother and 1 nephew, 1 sister had an illness "similar to the patient".

Past history at the age of 60 years of "cerebral arteriosclerotic dementia" which resolved in 5 months following admission to a mental hospital when pernicious anaemia was diagnosed. Liver injections were given regularly for only the past 2 years.

Present history of 7 years paranoid ideas, accusing people of thefts, and amnesia with exacerbation of symptoms in the past 6 months. Physical examination revealed gross arteriosclerosis. Hb. was 96 per cent., R.B.C. was 4.5 million, W.C.C. was 5,700 c.mm. and blood film was reported "suggestion of macrocytosis". "Hepostab" was given but no clinical change noted on discharge 4 months later.

Case No. 7

Mrs. E.W., aged 79 years. Family history of 1 cousin with "nervous trouble", 1 daughter "hysteria".

Past history at age of 69 years of a depressive episode following death of her grandson.

Present history of 2 weeks depression, insomnia and suicidal ideas following domestic friction. Hb. was 63 per cent., R.B.C. was 3.48 million and W.C.C. was 6,600 c.mm. "Cytamen" was prescribed and the morbid thoughts were rejected within 10 days of commencing treatment though her social situation preceding admission remained unchanged. On discharge Hb. was 80 per cent. and R.B.C. was 3.4 million, despite addition of ferrous sulphate and ascorbic acid tablets.

Case No. 8

Miss E. DeK., aged 57 years.

Past history of "nervous exhaustion" at age of 53 years and "melancholia" at the age of 53 years.

Present history of elation with unco-operative and aggressive behaviour. Hb. was 86 per cent., R.B.C. was 4.7 million. Patient had received monthly vitamin B₁₂ injections after a diagnosis of pernicious anaemia was made 5 years ago and she discharged herself from hospital within 3 days.

Case No. 9

Mrs. M. L., aged 68 years. Family history of 1 sister with a diagnosis of schizophrenia.

Past history 6 months ago of being "moribund" at home with absent vibration sense in legs and at that time her Hb. was 42 per cent., R.B.C. was 1.44 million, M.C.D. 8.7 μ ., and W.C.C. was 4,500 c.mm. Though receiving liver injections at home these were not regularly maintained.

Present history of 1 month's duration of depression, nihilistic delusions, guilt, restlessness and patchy amnesia with perseveration. Physically the patient showed evidence of arteriosclerosis and a B.P. of 205/115. "Hepalon" and "Cytamen" was given though the blood count was Hb. 94 per cent., R.B.C. 4.7 million and W.C.C. 5,000 c.mm. The depressive element responded to E.C.T. but the underlying dementia remained.

Case No. 10

Mrs. A.S., aged 64 years.

Past history of 1 month's duration of delusions of her leg being cancerous, talking to herself, paranoid ideas, disorientation and restlessness.

Physical examination revealed old rheumatoid arthritis and varicose ulceration of both legs. Hb. was 54 per cent., R.B.C. was 2.7 million, W.C.C. was 4,000 and a blood film was macrocytic. Massive "Cytamen" dosage was given and 2 months later the Hb. was 80 per cent. but no change in her psychiatric state had occurred. Full recovery with no residual abnormality followed treatment with 11 E.C.T.s.

Case No. 11

Mrs. I.B., aged 47 years.

Past history of being an ineffectual, complaining and self-centred personality with 8 years history of disseminated sclerosis.

Present history of exacerbation of personal traits. Physically absent knee and ankle reflexes with extensor plantar reflexes were noted. Hb. was 88 per cent., R.B.C. was 3.6 million, W.C.C. was 10,000 c.mm. and the blood film was macrocytic. "Cytamen" was given but a very limited psychiatric improvement followed and the patient died one year later of the complications of neurological disease.

Case No. 12

Mr. W.G., aged 64 years.

Past history of partial gastrectomy at the age of 53 years and a diagnosis of pernicious anaemia was made at the age of 61 years. He was maintained on 250 μ g. I.M. "Cytamen" monthly.

Present illness of 1 year's history of episodic loss of consciousness without convulsions, gradual loss of memory and initiative, social irresponsibility and ethical deterioration. Psychiatric examination showed that the patient was disorientated, was confabulating, had amnesia and euphoria. Physically, early bilateral cataracts and absent ankle reflexes were found. Hb. was 86 per cent., R.B.C. was 4.8 million and W.C.C. was 5,500 c.mm. Following "Cytamen" 1,000 μ g. I.M. for 2 weeks, the Hb. rose to 110 per cent. but there was little change in his psychiatric state, though he became less aggressive following Stelazine treatment. A.E.G. showed evidence of generalized atrophy and E.E.G. revealed mild generalized non-specific abnormality which showed some improvement 5 months later.

Case No. 13

Mr. B., aged 84 years. The patient was found wandering, disorientated, restless, aggressive and unco-operative. No adequate information from patient or other sources was available. Physical examination revealed generalized pupura more evident on the lower limbs and absent ankle reflexes, whilst the psychiatric diagnosis was dementia. Hb. was 30 per cent., W.C.C. was 3,600 c.mm. and the macrocytic blood film was reported. Following "Cytamen" 200 μ g. I.M. on alternate days a reticulocyte response of 18.4 per cent. was noted and 2 months later, despite vitamin B complex and ascorbic acid, the Hb. was 80 per cent. With Stelazine minimal psychiatric improvement occurred.

Case No. 14

Mr. L.B., aged 42 years.

Present history of 2 years of depression, feeling a failure, diminished libido and lack of energy which persisted despite psychotherapy and E.C.T. given at different times. Following a

complaint of dyspnoea his Hb. was found to be 47 per cent., R.B.C. was 2.0 million and W.C.C. was 3,100. Paraesthesiae were experienced in his legs. One week after commencing "Cytamen" a reticulocyte response of 11.0 per cent. was noted. Two weeks later the psychiatric state was normal though the paraesthesiae remained and 7 weeks later the Hb. was 94 per cent., R.B.C. was 5.4 million and W.C.C. was 5,000 c.mm.

Case No. 15

Mr. J.M., an Indian, aged 38 years.

Present history, 2 weeks duration with periods of confusion during which he had religious visions. Mentally he was disorientated, resistive and incoherent though lucid intervals would follow. Physical examination revealed glossitis, loss of vibration sense in the legs and absent right ankle reflexes. His Hb. was 56 per cent., R.B.C. was 2.4 million; a macrocytic film was reported and EEG showed a generalized non-specific abnormality. Seven days later following "Cytamen" injections (100 µg.) a reticulocyte response of 7.0 per cent. occurred and an almost complete resolution of the mental state was noted despite a Hb. of 48 per cent. On discharge 1 month later the Hb. was 88 per cent. Four years later an acute illness characterized by ideas of reference, visual hallucinations, awareness of an evil influence and elated mood occurred. Loss of vibration sense was still noted. Hb. was 83 per cent. and R.B.C. was 4.5 million. A diagnosis of schizo-affective disorder was made which resolved in 1 month concurrently with increased "Cytamen" dosage.

Case No. 16

Mr. C.H., aged 75 years. Family history of 1 brother who had a depressive illness at the age of 70 years.

Present illness of 4 years duration characterized by depression, irritability and inability to work which responded partly to 2 courses of E.C.T. Present admission precipitated by 2 suicidal attempts. Mentally he was depressed, retarded and hypochondriacal. Physically, evidence of thickened arteries was noted. Hb. was 52 per cent., R.B.C. was 2.2 million and W.C.C. was 9,100 c.mm. "Cytamen" and "Campalon" was given with a rise of Hb. to 86 per cent. and R.B.C. of 4.0 million after 8 weeks with no psychiatric change of note. Considerable but not complete clinical response occurred following 10 E.C.T.s. The Hb. was 94 per cent. on discharge 9 weeks later.

Case No. 17

Mr. G.B., aged 64 years.

Present illness of 9 months duration characterized by depression, loss of weight, insomnia, indecisiveness following his mother's death and associated with fiancée's insistence on marriage. Mentally, he was depressed, irritable, retarded and mildly amnesic. Physically, his liver was firm and palpable, diminished knee reflexes, absent ankle reflexes and loss of vibration sense in his legs were recorded. Hb. was 60 per cent., R.B.C. was 1.6 million, and a macrocytic film was reported. In addition X-rays confirmed a clinical diagnosis of gout. Six days after commencing "Cytamen" a reticulocyte response of 15.5 per cent. was recorded. Almost complete resolution of the psychiatric state was apparent prior to the diagnosis of pernicious anaemia and was related to separation from a demanding fiancée. He was readmitted 9 months later for two days during which complete resolution of a transient depression with paranoid ideas occurred. The latter followed a general hospital admission for treatment of a fractured leg. Hb. was 92 per cent., R.B.C. was 4.4 million. No neurological abnormality was found.

Case No. 18

Mr. C., aged 62 years.

Past history of depression at the age of 56 years successfully treated with E.C.T. One year later depression associated with pernicious anaemia. treated with liver injections.

Present history of 6 months duration of depression, hypochondriasis, weeping, self-reproach and inability to work. Physically, his liver and spleen were palpable, bilaterally absent ankle reflexes were noted with absent deep sensation in the right leg. Hb. was 75 per cent., R.B.C. was 3.2 million, and a macrocytic blood film reported. Three weeks after commencing "Cytamen" marked mental improvement occurred despite lack of improvement in neurological state and sub-optimal blood count.

Case No. 19

Mr. R.D., aged 46 years. Family history of father and 2 brothers being "drunkards". The patient had a long history of excess alcoholic intake (15-20 pints of beer daily) with recurrent hallucinosis resolving with abstinence. A diagnosis of pernicious anaemia was made 2 years previously and the patient received injections of liver regularly.

Present illness of 7 weeks depression hearing voices and still drinking heavily. Physically, motor weakness was present in both legs with impairment of touch and pin-prick sensation and diminished reflexes left arm and leg were noted. No evidence of dementia was present. Hb. was 84 per cent., R.B.C. was 4.2 million and a mild degree of macrocytosis was reported.

One week later he was mentally normal and the Hb. was 85 per cent. In view of his past psychiatric history the improvement, concurrent with the giving of "Cytamen" appears coincidental.

Case No. 20

Mr. A.P., aged 62 years.

Past history of being invalided out of the army during 1914-18 war on psychiatric grounds.

Present illness of 1 year's duration characterized by depression, hypochondriasis, restlessness, impotence and work deterioration. On admission Hb. was 90 per cent., and R.B.C. was 4·8 million. Physically, his B.P. was 180/115 and vibration sense in legs was absent. A diagnosis of pernicious anaemia and depression was made elsewhere when the patient was 54 years, no neurological signs then being present. His psychiatric state gradually improved during the following months with recovery of potency.

CO-OPERATION IN WORLD MENTAL HEALTH YEAR

By

J. R. REES, C.B.E., M.D.

Director, World Federation of Mental Health

I AM glad that the Papers Committee has arranged today's meeting in order to give some emphasis to the international aspects of preventive psychiatry and work for mental health. Faced continually with the pressing needs of our own individual professional tasks, it is wise sometimes to raise our sights and look at some of the problems and activities of our neighbour countries in the world.

Our Association was of course one of the twenty-two Founder Members of the World Federation for Mental Health when it was inaugurated in the Ministry of Health, London on 18 August, 1948. The R.M.P.A. then became a member of an inter-professional organization which, in addition to many psychiatric bodies, includes psychologists, sociologists, anthropologists, nurses, teachers, and other groups of professional people concerned with the behavioural sciences, as well as many national and local mental health associations.

The concept which we had at that time is, I believe, still true, that whereas therapy is primarily the responsibility of the medical profession, health—physical, mental and social—demands the thought and work of a team representing many disciplines.

The Federation has grown, and now has 124 member associations in 43 countries. I would remind you that the only other body concerned with international problems of mental health is the Mental Health Section of the World Health Organization, which is a Specialized Agency of the United Nations, an inter-governmental body which acts primarily through governments, and which incidentally has done much outstanding work through its Expert Committees, its consultant services and its arrangement of fellowships. W.F.M.H. works very closely with W.H.O., as also with the Social Science and Educational Departments of U.N.E.S.C.O. We have consultative relations with the Economic and Social Council, with I.L.O., and with U.N.I.C.E.F. in addition; and in our close contacts with all of these bodies we are able very often to give needed emphasis to the psychological or mental health aspects of many problems that are under discussion, which might otherwise be overlooked.

I will not weary you with a recital of what your Federation has attempted or has done during the past eleven and a half years. Some of you, though by no means all, are individual Associates of the Federation, and therefore have been kept in closer touch, through its journal, the annual reports, etc. I would, however, just remind you that the Federation, working on a minimal budget, has in fact accomplished quite a lot. It has been a clearing-house for information in this field to a growing extent, able to answer at least some of the many questions that are posed, able to create contacts between people with similar interests in countries on opposite sides of the earth. It has stimulated the creation of many new psychiatric and mental health groups in countries where none existed, and in fact there are at least a dozen countries or territories

where such activities are going on now which are not at present in membership or included in the 43 countries that I have mentioned. There are, for example, three active societies in Yugoslavia, eight or nine scattered on the Caribbean islands, a number in Asia, the most recent being the society created two months ago in South Korea, and there are a number in process of formation in the territories of Central Africa, where the problem of isolation of native and expatriate psychiatrists and social scientists has been a major one, in which we, with the co-operation of the Council for Technical Co-operation in Africa South of the Sahara and the World Health Organization, have succeeded in creating new activity.

International meetings are perhaps more meaningful in many areas of the world than they are in an over-privileged country like this. It is certain that our annual meetings, held in different countries, with the opportunity for small friendly discussion groups, have done much, through the creation of contacts and the sharing of problems and the description of successes and failures. Similarly, the Regional Meetings that we have held for the officers of member associations in Scandinavia and in Central America have had marked results in the continuing organization, co-operation and progressive development of work in those regions.

International teaching seminars for those who are themselves teachers of others in their own country have achieved much. The two notable ones for which we have been responsible have been that at Chichester in 1952, and that in Manila at the end of 1958.

The hard-working Scientific Committee of the Federation produced its first paper, *on Identity*, two years ago, and in pursuance of its aim to clarify some of the basic elements involved in the concept of mental health, it is just about to publish its second monograph, *on Mental Health and Value Systems*, which has necessitated much hard work, and conferences with representatives of the different religions and ideologies of the world.

The Federation has held a number of special expert conferences: on Student Mental Health, on Research in International Communication, and on the Methodology of Attitude Surveys.

Pre-arranged consultant visits have been paid to some 98 countries or territories in the world, and though some of these have been brief, such evaluation as we have been able to achieve shows that they have in fact been productive, and have played their part with governments as well as with purely professional workers in changing the climate of opinion with regard to the care and treatment of the mentally sick, and the activities that are necessary for the prevention of the less dramatic forms of mental illness.

We have carried out a number of projects at the request of W.H.O. and U.N.E.S.C.O., and many for ourselves. We are at the moment completing a small survey in 14 countries of the psychological problems in general hospitals. We have a project which aims to improve the selection procedures for the international Secretariats of U.N. and for those going on overseas technical missions. In the United States we are responsible for a study of the rehabilitation of discharged mental hospital patients, which has government support, and we are planning a conference particularly to help F.A.O., W.H.O., U.N.I.C.E.F. and P.A.H.O. on the psychological and cultural factors which create difficulties in the changing of food habits.

This, of course, is not by any means a complete list, but it gives you a quick look at some of the interests which your Federation has been encouraging over the years.

World Mental Health Year 1960, which we announced in 1957 at the annual meeting in Copenhagen, is by far the largest and most ambitious project of the Federation. The steadily increasing awareness of the problems of mental ill-health and the need for attitude changing in all parts of the world which had grown up amongst the government administrators, largely as a result of the educational work of W.H.O. and the Federation, was one of the factors in deciding the Executive Board of the Federation to take this step. The other factor was the apparent increase (apparent, because of the total lack throughout the world of reliable figures from past years) in anxiety and other neurotic conditions, and the increasing evidence of psychotic illness, due probably to the growing failure of family and tribal groups to contain people who are exhibiting abnormality or deviant behaviour.

Two-thirds of the world's population have never known anything but hunger, and it will be long before this situation is changed. The decrease in infant mortality, the increase of populations, and the difficulties in the development of agriculture, are all factors here. One of the crucial points, however, is that knowing that better things can be achieved, the under-privileged countries all over the world are trying desperately to raise their standard of living by mechanizing their agriculture, by commencing industrialization, and the general modernization of their form of life. A factor such as the change-over from a barter economy to a money economy is in itself a disturbing element, but the change of occupation following on improvement in the means of communication and the rapidly increasing urbanization is an even greater disturbance to the culture patterns of most countries. Because of these factors, and because of spreading education of young people in languages which mean that they cannot easily communicate with their parents, the joint or extended family system which has operated for so many years in Asia and in the Latin-American countries is breaking down, as is the tribal system of organization in Africa. This creates what Erikson has called "identity confusion", and anxiety arises for this reason, added to by the stresses of not getting a job at monetary rewards which they hoped for, fears of losing a job, the critical situations that follow the loss of a job, and the "keeping up with the Jones's" which is common to every country in the world, under whatever name the Jones's may be known.

The general hunch (and it is no more than that) which Western-trained psychiatrists working in under-privileged countries have, is that probably there is no change in the actual morbidity due to psychosis, but there seems no doubt that there is a true increase in neurosis, and this creates a very challenging problem for our times. It is something for the solution of which all of us must attempt to carry some part of the responsibility.

The development of our own psychiatric services, the improvement of our teaching, the intensification of our research, are all extremely necessary things—for our own country, but also in order to enable us to provide some kind of basic data and concepts which can be made use of by countries of less sophistication and far less good facilities. Nigeria, with 32 million people, has one psychiatrist. The Sudan, with 20 million, has one psychiatrist. Some parts of the British colonial territories have no psychiatrist, and their methods of dealing with the mentally disordered are almost indescribably primitive. The People's Republic of China a few years ago had a maximum of ten psychiatrists, and at the present time have apparently trained some three hundred or so since we have separated from them, but how far is this likely to go in meeting the problems of 630 million people, where already the Ministry of Health in Peking has declared mental breakdown as a first priority?

It was because of matters like this that it seemed entirely appropriate to try and stimulate scientific thinking and wise educational and social action for better mental health throughout the world. It is unrealistic to believe that psychiatrists and psychiatric facilities can be provided sufficiently to deal with the problems that face our few colleagues in all these under-privileged countries. Prevention must, I think, be the long-term answer, and prevention must be along the well-established lines of public health practice.

In passing, one may point out that the eradication of malaria, yaws, syphilis, leprosy, etc., is something which is fairly easy to understand, both for doctors and for laymen. These are killer diseases. We have in our own field one example of a killer disease which is in the main our responsibility, about which we do remarkably little. That is prejudice, which has always existed in every country in some form or other as an endemic disease with epidemic outbursts. It killed six million people in Europe not long ago. It is in part an economic, social and political disease, but whose responsibility is it to discover how prejudice begins and how children are to be brought up with a positive sense of pride in their own identity so that they will be resistant to infection by prejudiced ideas as they go through their early life at home and at school?

The general plan for World Mental Health Year, as you will know from the literature, was that we should aim primarily at the scientific approach and the discovery of validated factual material upon which preventive work could be undertaken through education or social action. Some few countries of the world will probably need popular instruction, but this was not a primary aim of W.M.H.Y. There are two major elements in the programme: first, the assessment in as many countries as possible by the people on the spot of the high priorities of their own country in the field of mental health, so that they could devise new national programmes or give increased emphasis to existing activities; and secondly, a small group of topics picked out of the many possibilities which might be regarded as central international matters of interest where data and material could well be exchanged over national boundaries, and where we could learn a very great deal from the successes and failures of people in all countries.

This is the plan that we have pursued, and in doing this, by communication of course with your fellow member associations, with the government Ministries of Health, Education, Social Welfare, and Justice of every country in the world (in five languages), by drawing in the interest of other international non-governmental organizations like ourselves, we have discovered that we have created a ferment, because there clearly was nearly everywhere a recognition of the need for such work. We know now of over 150 projects which have either been offered to W.M.H.Y. or have started as a direct result of our activities, and some 50 or 60 of these merit being called scientific activities—research, surveys, etc.—whereas the others are largely action projects.

The central projects were originally five, and we have now added a sixth. In brief, they are: (1) needs of children and youth; (2) stimulation and carrying out of attitude and morbidity surveys in the field of mental health; (3) establishment or improvement of fundamental education in the principles of mental health in all related professional schools everywhere; (4) determination of methods by which help can be given to industrializing countries to avoid some of the mistakes made by the developed countries, so that industrialization shall make a contribution to good mental health, and not the opposite; (5) psychological problems of migrant populations and refugees; and (6) the gerontological problems which arise, and which will of course be obvious in the studies of projects (2) to (5).

These are certainly all major projects which in our original planning we decided would demand a period of at least four years, though (as we hoped) starting in 1960. Each of them involves a first year of fact-finding upon which the detailed programmes of future action will have to be based; each demands groups of people in many cultural and language areas of the world co-operating. For each of them we have for some time had the consultants or co-ordinators who are willing to take on responsibility for doing all that can be accomplished in each of these fields.

The estimated cost of our original plan for the five projects, on a four-year basis, came to $2\frac{1}{2}$ million dollars—some £900,000, and we have so far failed to find funds of this magnitude available. We have, in fact, only a minimal fund. Despite this, the Executive Board of the Federation and we in the Secretariat are by no means disheartened. We have a great deal of voluntary work going on towards the achievement of the goals of these five projects. Some of our special consultants are working part-time for nothing. Two of them have been working on their particular themes while in the employment of W.H.O. One of them is, while waiting, the Adviser on Mental Health for one year to the High Commissioner for Refugees. Five highly competent U.S. workers are devoting their sabbatical leave to work on various aspects of these projects, and there are at least two offers from this country of similar work which we hope to take up. Many of the national projects will result in a direct contribution of substance to these central projects. While we still must look for much larger support, we are sure that with patience a great deal will be achieved, even with a minimum of finance.

World Mental Health Year has from the beginning been announced as something which is not just an activity of the Federation, but something which welcomes and involves anybody and everybody in the world who has a serious interest and concern in these matters. We have the co-operation and sponsorship of W.H.O., excellent co-operation from U.N.E.S.C.O., first-rate co-operation from C.C.T.A., the inter-governmental body in Africa who have already helped with the African conference, have held an expert meeting on the Development of the African Child, and are holding two more meetings, one on Aptitude Tests and the other on The Adaptation of Education to African Needs—all as a part of their contribution to W.M.H.Y. Many government bodies in different countries are co-operating with a good deal of enthusiasm. Very encouraging speeches have been made in the Senate and the Congress of the U.S. President Eisenhower has sent cordial messages. The Presidents of Austria, of Finland, and of a number of other countries in Europe have taken their part in the inauguration of W.M.G.Y., and our Latin colleagues have followed their admirable habit, and there have been Presidential Decrees that World Mental Health Year 1960, is official in Peru, Argentina, Venezuela and Cuba. Costa Rica and Spain are to follow in this.

As you will see even from so partial a recital of both scientific and public interest in W.M.H.Y., we have all of us some reason for being stimulated. The leaven is working in the lump.

And now, what do we in the R.M.P.A. do about it? The N.A.M.H. and the Scottish Association for Mental Health, and the Committee which represents the eleven member associations in this country, have already stimulated a great deal of interest in the on-going national programmes and in the stepping up of new activities in the United Kingdom. Social welfare organizations in considerable numbers are joining in with special issues of their journals, special meetings, etc., and now that we have Refugee Year (which gate-crashed to some

extent, but which does not in fact clash) reaching its later stages, there will be, I hope, more sensible publicity in this country.

Everyone must decide for himself what particular kind of activity can be undertaken, but I would suggest that we think not only of the needs of our own country, which are many, but also of the value and utility of what we can produce, either by research or by the distillation of our clinical experience which can be of value to our colleagues in neighbour countries throughout the world. We should know basic facts which are proven, on which we can devise prophylactic methods and new techniques for ensuring the health and stability of future generations. It is not always easy to separate out from the work we are accustomed to do in our local setting those things which may have more universal applicability. I would ask you whether you cannot produce statements about your findings which are simple and not only related to the local scene, and our own type of organization, but which can be adapted or adopted, or at least considered carefully, by your colleagues in a hundred or more countries in the family of nations.

This is what we need above all, and my hope is that this country, which of recent years has been giving a lead to the world in the care and treatment of the mentally sick, can provide a great many ideas which can be applied prophylactically throughout the world. This is the form of technical assistance that we can provide; perhaps also evidence that we can be a Great Nation, the quality of whose work of all kinds can influence world society.

The efforts of Israel in modifying the laws with regard to sexual assault of children, so that youngsters no longer have to appear in court, and thereby avoid an increased sense of anxiety and guilt, is but one instance of social action taken on the basis of something that all of us have known, but none of us had taken action about.

We shall certainly need more validation of the theories about separation anxiety in children if we are to have something to compare with the opposing ideological concepts in this field of the Socialist Republics of Europe, or the experience of the Kibutzim in Israel. Every region of the world will need to try to formulate its concepts of psychiatric practice and the principles of mental health, and these will be different for Asia, Africa, Latin America, the Socialist Republics, and the so-called West. We shall learn much from discussions and comparisons of the varying methods with their very different cultural backgrounds, and the evaluations that can be produced.

I need say no more, I think, except that World Mental Health Year needs your interest, your comment and criticism, and above all, your work.

THE EFFECTS OF NICOTINIC ACID, NICOTINAMIDE, AND PLACEBO ON THE CHRONIC SCHIZOPHRENIC

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FOR various reasons we became interested in the possibility that nicotinic acid or nicotinamide might be of some benefit to the chronic schizophrenic. Many workers have noticed clinical similarities between the acute schizophrenias and the encephalopathies of nicotinic acid deficiency (4). Nicotinic acid is known to be of value in pellagra (2) and in the treatment of delirium tremens and allied states (1), and Osmond and Hoffer have had promising results with these substances in the treatment of schizophrenia in its acute phase (3). There seemed therefore to be sufficient reason for an investigation of their effects in the schizophrenic in the chronic phase, for, as far as we are aware, the therapeutic possibilities have not been explored. Since patients often respond strikingly to the giving of any tablet, regardless of its contents, we also gave similar tablets of an innocuous substance, here referred to as Placebo. For convenience the three preparations employed will be referred to in future as *A* (Nicotinic Acid), *M* (Nicotinamide) or *P* (Placebo).

THE TEST

The group tested consisted of chronic schizophrenics, of ages from forty to seventy.

The design of the test was arranged so that certain errors were avoided. One of these was that different patients would tend to be at different clinical levels throughout the test. This fact can be allowed for by giving all three treatments to each patient, and then making comparisons only between results from the same patient, by taking differences say, so that each patient acts as his own control.

Another error is introduced by secular changes, whether by the patient being at first stimulated by the mere fact of being given something, or by the clinician's standard of what is "good" changing slowly throughout the test. These errors were avoided by testing the patients in triples, in which one patient

received the drugs in the order *A, M, P*, while the other two received them in the orders *M, P, A*, and *P, A, M*. Thus each substance occurred once in the first place, once in the second, and once in the third. The *sums* over such a triple have the errors balanced out.

Such a set of three patients, chosen to be as alike as possible in age, clinical condition, sex, past history, etc., formed the primary block for the test. From this block the basic information that we require is obtainable. Random sampling was then reduced as far as was possible by the provision of further blocks, each as homogeneous as possible internally. Thirteen such blocks went through the test to completion, involving thirty-nine patients. Thirty patients (ten blocks) were of women, nine (three blocks) of men.

Some time might be necessary for the treatment to show its effect, but we considered that eight weeks on each substance might well be sufficient for any action to declare itself. Accordingly each substance was given for eight weeks continuously. One week without treatment was allowed between each eight week period; so the patient was under observation over twenty-six weeks in all.

In each eight-week period on one substance, the first week was used to raise the dosage to its maximal level. Three hundred mg. t.d.s. was given on the first day and each day the dosage was increased by this amount so that on the seventh day the dosage was 2.1 grams t.d.s. (i.e. 6.3 grams per day). This last level was then sustained for seven weeks.

ASSESSMENT

We were interested chiefly in the patients' *general clinical condition*, rather than in their response to specialized psychological tests (and in any case the chronic schizophrenic would often be quite unco-operative in the employment of any special tests). So we assessed the patients' clinical state by the following twenty-three criteria:

- | | |
|---------------------------------|--|
| 1. Does he have to be fed? | 13. Has he been dirty in his habits? |
| 2. Has he been mute? | 14. Is he deluded? |
| 3. Has he talked to himself? | 15. Has he masturbated? |
| 4. Does he sleep badly? | 16. Is he destructive? |
| 5. Does he daydream? | 17. Is he suspicious? |
| 6. Does he keep to himself? | 18. Is he hallucinated? |
| 7. Does he laugh without cause? | 19. Is he homicidal? |
| 8. Is he apathetic? | 20. Is he suicidal? |
| 9. Is his behaviour childish? | 21. Has he been impulsive? |
| 10. Is he upset easily? | 22. Does he employ himself in any way? |
| 11. Is he untidy in his dress? | 23. Has he any interests? |
| 12. Does he hoard rubbish? | |

Each question was answered by "Yes", "No" or "Variable". At the end of each fortnight the patient was assessed by the twenty-three questions, and a score derived. One point was given for each "Variable", two points for each "No" occurring in the first twenty-one questions and two points for each "Yes" occurring in the last two questions. Thus the maximal score at one assessment was 46; a high score corresponded to a good clinical condition.

The questionnaire was filled in by the Ward Sister who had had the patient under observation during the previous fortnight, in consultation with the psychiatrist. Each patient, over the twenty-six weeks, was thus given twelve assessments of his condition.

To ensure that the person filling in the questionnaire was unbiased, the three drugs were given in an order known only to the dispenser, who allotted one of the three orders mentioned above to each of the three patients. Thus

the person marking the questionnaire would know, on a particular week, that one of the patients was on nicotinic acid, one on nicotinamide, and one on placebo, but she would have no way of telling which was which other than by whatever was clinically observable.

In all, thirty-nine patients contributed to the test by completing the course. Although the whole group was, naturally, somewhat heterogeneous, the blocks of three were so arranged that each block was fairly homogeneous internally. As will be shown below, all the comparisons were made primarily within the blocks; thus the comparisons are based on material much more homogeneous than the total range of patients in the group.

RESULTS

It is convenient first to dispose of some minor matters. The thirty-nine patients mentioned above were those remaining after nine patients had refused to continue the treatment. One patient refused while receiving the acid, six during the amide, and two during the placebo. Although the refusals were mostly against the amide, the multinomial distribution shows that, as the probability of exactly one, two, and six is 56/729, i.e. about 1/13, the difference can hardly count as significant.

Nicotinic acid is, of course, well known to cause vaso-dilation. Each form recorded whether flushing had occurred, and the occurrences were divided into "slight" and "marked". The three substances gave flushings as shown in Table I

				TABLE I			Degree of Flushing		Total
				0	Slight	Marked			
Acid	..	..	..	106	42	12			160
Amide	..	..	..	146	13	1			160
Placebo	..	..	..	137	18	5			160
Total				389	73	18			480

Table I includes the results for one patient who completed the course but whose Block was not completed.
 χ^2 is 36.7; n=4; p is less than 0.001.

It is clear that the nicotinic acid produced flushing much more than the others. One cannot help noticing, however, that the nursing staff, otherwise highly trustworthy, have recorded flushing in no less than twenty-three occasions when the patient in fact was on placebo. We do not regard this as a suggestion that the staff was unduly careless; we regard it rather as showing how essential it is that any question involving some degree of judgment should be made in ignorance of the factor at work.

We can now turn to the main matter of interest: whether, if the drug acts quickly, the general level of clinical condition tends to be better on either of the two drugs than on the placebo.

For this purpose the four scores (over the 8 weeks under each drug) were added together. Thus, each patient now gave three totals, one for acid, one for amide and one for placebo occurring in some order. The three patients in a block each gave three results, forming a Latin square. Thus, patients Nos. 13, 14 and 15 gave the scores shown in Table II, where the columns show the three periods, and the letter after each entry shows the drug given.

TABLE II

Patient No.				Period		
				1	2	3
13	..	..	..	127 (<i>A</i>)	121 (<i>M</i>)	118 (<i>P</i>)
14	..	..	..	95 (<i>M</i>)	108 (<i>P</i>)	109 (<i>A</i>)
15	..	..	..	134 (<i>P</i>)	176 (<i>A</i>)	174 (<i>M</i>)

The difference between rows represents the fact that, e.g., patient 15 was consistently in a better clinical condition than patient 14. The difference between columns reflects the fact that secular changes (such as a drift in the markers' standards) might be occurring. The other differences show the usual effects of treatment or of interaction. Thirteen blocks provide the necessary replication.

The analysis of variance of the 117 observations need not be given in detail. The essential part occurs in Table III, which gives the totals for the treatments.

TABLE III

			Period		
			1	2	3
1,504 (<i>A</i>)			1,504 (<i>A</i>)	1,641 (<i>M</i>)	1,590 (<i>P</i>)
1,525 (<i>M</i>)			1,525 (<i>M</i>)	1,687 (<i>P</i>)	1,654 (<i>A</i>)
1,610 (<i>P</i>)			1,610 (<i>P</i>)	1,705 (<i>A</i>)	1,736 (<i>M</i>)
$A=4,863$	$M=4,902$	$P=4,887$	$F_1=4,927$	$F_2=4,005$	$F_3=4,820$

It also gives (as *F*'s) the three diagonal totals whose differences represent high-order interactions. What interests us especially are the differences between the totals for *A*, *M*, and *P*.

The eight degrees of freedom in Table III can be divided into the following:

1. Two degrees of freedom between columns; these are of no interest since they represent secular changes in the experiment, and are required only for elimination.

2. Two degrees of freedom between rows; these represent differences between three sets of 13 patients, and are required only for elimination.

3. Two degrees of freedom between the treatments *A*, *M*, and *P*. These may meaningfully be divided into one degree of freedom which compares the condition under placebo with the average condition under acid and amide, and one degree of freedom which compares the acid and the amide.

4. Two degrees of freedom due to high-order interaction; they are represented by the variance between the three totals *F*, and provide the appropriate estimate of error.

The analysis is shown in Table IV

TABLE IV

Variance					D.F.	Sum of Square	Mean Square
Acid v. Amide	..	..	..	..	1	19.5	19.5
Placebo v. Drug	..	..	..	..	1	0.3	0.3
Rows	..	..	..	..	2	1292.7	—
Columns	..	..	..	..	2	2344.7	—
Interaction	..	..	..	..	2	163.8	81.9
Total	..	..	..	..	8	3820.9	—

In the Table the divisors used in forming the sums of squares have been those appropriate to the full analysis of 116 degrees of freedom.

The results in the right-hand column show unequivocally that there is no evidence for any change in the clinical condition so far as a general change in the level is concerned. "Drug" is not significantly better than placebo, and the two forms of the drug show no significant difference.

There remains the possibility that the drugs may have had a cumulative effect, so that the clinical condition at the end of the eight weeks' treatment was significantly different from that at the beginning. This question can be examined simply by using, as the estimator over the eight weeks, not the sum of the four scores but the difference between the last and the first. The difference under nicotinic acid can then be compared with that under the amide, and so on. The null hypothesis is then that these quantities are normally distributed about zero, so *t*-tests are appropriate. Again the two main matters of interest were:

1. Whether the change under placebo differed significantly from the average change under the drugs (within each triple);
2. Whether the acid and the amide differed in the amounts of change they produced.

T-tests showed, in fact, that both the changes were insignificant.

SUMMARY

The effects of massive doses of nicotinic acid and of nicotinamide were tested on the chronic schizophrenic, together with an inert placebo. Thirty-nine patients were tested, each over 24 weeks. The results were assessed on a prepared scale.

Analysis of the results failed to show any evidence that the treatments were influencing the patients.

ACKNOWLEDGMENTS

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THE ROLE OF EXTRA-SENSORY PERCEPTION IN EARLY CHILDHOOD

By

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INTRODUCTION

IN this paper I do not propose to argue the case for or against the existence of telepathy and other forms of E.S.P., but will simply content myself with two quotations concerning the matter.

In reviewing Soal and Bateman's (1954) book *Modern Experiments in Telepathy* in the *Journal of Mental Science* of January, 1955, Ross Ashby says: "the evidence he" (that is Soal) "has produced is very strong, strong enough to give ample justification for a belief in telepathy." And again: "Exclusion of every conceivable source of small bias is not easy, and those who wish to support the verdict of 'not proven' are in no way unreasonable. The position, in fact, is still uncertain. The evidence is very strong—there is no question of that—but one may still doubt if it is absolutely conclusive." He ends by comparing the position with that "occurring 150 years ago in the phenomena of electricity". He says: "At that time only one or two phenomena were known, the relation between them was obscure, and it could be asked contemptuously what connection could rubbed amber possibly have with a frog's twitches? Neither of the phenomena were regularly reproducible, and they doubtless often refused to appear when a special demonstration was staged; (for the occasion would lead to variations in method that were unwittingly fatal to the demonstration, for no one knew what was important). The little that was known about the phenomena made no sense in terms of the science of the day, which recognized only gravitational, mechanical and chemical forces. The phenomena were trivial, and there were plenty of 'ordinary' explanations that might have explained them. 'Electricity' in those days was not, scientifically, a respectable subject. It may be that these telepathic and other phenomena are similarly just straws that show the movements of an otherwise unobservable atmosphere."

For my own part, I am convinced both by my personal experiences and by my reading of the existence of telepathy and of clairvoyance, and throughout the remainder of this paper I shall assume that they do occur as objective phenomena.

WHAT IS E.S.P., AND HOW DOES IT TAKE PLACE?

Firstly then, what is the nature of telepathy? In his paper "Telepathy in Analysis", published in 1947, Fodor says: "it might be nearer the truth to postulate telepathy as a cognitive faculty of the unconscious, shared by humans and animals alike", and I think most workers in this field would probably accept his formulation.

Freud in 1933 had suggested that telepathy may be simply "the original archaic method by which individuals understand one another, and which has been pushed into the background in the course of phylogenetic development

by the better method of communication by means of signs apprehended by the sense organs."

Jan Ehrenwald (1947) in his book *Telepathy and Medical Psychology*, stresses the "primitive vestigial nature of telepathy". He says: "It suggests that, apart from giving a distorted picture of processes in another person's mind, telepathy is also apt to reflect them with utter disregard of their temporal order." Pointing out that "such reactions . . . are totally undesirable from the biological point of view", he uses Thouless's (1942) illustration of "the embarrassment of a deer" which had to rely on E.S.P. to make it aware of the presence of a tiger. He says: "It would be unable to decide whether this danger referred to a tiger in the vicinity now, to one a hundred and fifty miles away, or to one that would be there tomorrow. And to this we have to add that if it were a deer conversant with the subtleties of Freudian symbolism it could not even be sure whether the animal was a tiger at all and not a veiled intimation of sexual aggression."

Earlier in the same book, Ehrenwald states: "But our observations show at the same time that there is an ingrained tendency in our mental make-up which militates against the intrusion of hetero-psychic influences into our mind, a psychological diaphragm whose business it is to prevent the occurrence of telepathy and which subjects such hetero-psychic material as may penetrate through the diaphragm to . . . forces of repression . . . Whatever the meta-physical nature of personality, there can be little doubt that the tendency just described is one of the essential pre-requisites of its existence. Its failure to maintain its protective screen entails mental derangement. Its complete break-down leads to the break-down of the personality, whilst a transient permeability of the screen to certain patterns of psychological processes may lead to such occasional telepathic occurrences as we have seen during casual absent-mindedness or in states of minor emotional disturbance."

He suggests that telepathy occurs either as compensation for some defect in the channels of conscious communication, which defect he refers to as a "minus function", or as what Hughlings Jackson described as a "release phenomenon". Referring to states of motor excitement associated with sudden death, Ehrenwald says: "It is interesting to recall here that Hughlings Jackson, the great English neurologist, attributed reactions of this class to the sudden release of the activity of primitive strata of the central nervous system, accompanying the dissolution of the higher strata. In fact, his strata theory has gone far to explain a wide variety of symptoms, both neurological and psychological, along the same lines. The relevance of this Jacksonian doctrine to our problem is obvious. It suggests that so-called telepathy from the dying can be explained in terms of Jackson's release phenomena, and it may well be that what we said on an earlier page, regarding the part played by emotional factors, psychological crises, etc., in the mental setting of the agent, may likewise be accounted for by his theory. *Mutatis mutandis*, the same may be true for what we described in such minus-states on the part of the percipient as sleep, mental dissociation or special disabilities, and their corresponding tendency to compensation."

Throughout the remainder of the book, however, Ehrenwald tends to adopt the hypothesis of E.S.P. as a compensation, whereas I prefer to regard it as a release phenomenon, although the released lower-level function may of course act as a partial compensation for the impaired higher one.

It should be noted that the "defect" in the higher, inhibiting level need not necessarily be an innate nor even a physical one, nor need it be permanent. It may be intermittent, as in the case of fatigue, for example, or it may be due

to emotional disturbance having produced an inhibition of or a regression from the higher-level function.

It is clear that E.S.P. acts independently of both space and time. In trying to explain this fact, Ehrenwald (1954) says: "we have to give up the idea of a punctiform, ego-centric, uni-cerebral localization of 'consciousness' and adopt the theory of a potential *multi-cerebral* or *scattered* localization of mental processes. To put it in other words: we have to conceive of human personality in terms of a potentially open system . . . , or rather of a personality field sweeping across the boundary lines of strictly isolated individual units . . . It can be argued that our thesis is little more than a mere elaboration of the fact of heteropsychic experience, in contradistinction to what we described as autopsychic experience. We may be told that our formulation still leaves us in the dark as to the way in which we become aware of heteropsychic experiences. But we have to realize at this point that we are faced with the identical difficulty when we try to answer the same question in regard to the autopsychic sphere."

It may be objected that these two phenomena are not truly comparable since autopsychic experiences are accompanied, we believe, by simultaneous changes in the brain. If so, I would draw attention to the paper by Professor J. C. Eccles in *Nature* of July, 1951 (referred to by Soal and Bateman in *Modern Experiments in Telepathy*), in which he suggests that certain neurons in a critical state can be fired by some external influence which seems to be of the nature of psychokinesis.

I think this is as far as we can go at the moment towards the solution of this particular problem.

PHENOMENA WHICH CAN BE MOST SIMPLY EXPLAINED BY POSTULATING THE OCCURRENCE OF TELEPATHY

In 1935, Dorothy Burlingham described four or five incidents of apparent telepathic communication between mothers and their children, saying that these illustrated "a phenomenon which demands investigation", and probably we all know of mothers who complain that their babies are never fretful except on the rare occasions when they themselves are planning to go out later in the day without the child, but before they believe themselves to have given any sign by which the infant could be aware of this. In addition, there are certain groups of puzzling phenomena which can be satisfactorily explained by the hypothesis of a free and universal occurrence of telepathy between mothers and their young children. I am referring to the existence of what appear to be memories of events which occurred in very early life, of inherited memories, of certain apparently innate knowledge, and of the undoubted response of young children to unconscious emotional attitudes in their mothers.*

(a) *Early Memories*

In his book *Pygmies and Dream Giants*, Kilton Stewart (1955) describes a method of psychotherapy practised by the Negrito pygmies of Luzon. Having himself hypnotized one of their men called Pana, who suffered from recurrent headaches, and asked him to go back to find when he "first met the headache spirit", Stewart discovered that this was in fact the traditional procedure used by the Negritos' own shamans, several of whom joined him in instructing the

* For a full discussion of some of these, and for a bibliography, see Ehrenwald's *New Dimensions in Deep Analysis*.

patient what to do, "which", as he puts it, "resulted in group psychotherapy in a new sense—a group of therapists working on one patient".

He states that the man gradually curled up and began to groan and writhe. Presently he said he was as yet unborn when he first felt the pain. Stewart's interpreter explained that Pana's spirit had now gone back to the cave in a high cone-shaped mountain in the north in which he lived before he was born. The patient then described how he had heard a quarrel between his parents and also the sound of thunder and said that it was these which had first caused his headaches. Stewart comments that the Negritos accepted these statements without surprise. When Pana came out of the trance, he said he felt better.

This method of treatment is, of course, very similar to and obviously much older than the technique of "Age Regression" under hypnosis used by Erikson and Kubie (1941) and by Wolberg (1945) and others. Kelsey (1953) has described similar recall of birth and pre-conception "memories" under hypnosis, and Sandison (1954) and his colleagues using LSD (d-lysergic acid diethylamide), have had several patients who described their own birth, but some of them, Sandison says, "have thought themselves to be their own mothers and two such patients went through the experience of their own births, with dramatic and characteristic pains and movements". Lastly, Hubbard's (1950) *Dianetics* might be mentioned here. In that system it is claimed that the subject is carried back on the "time track" to recover pre-natal and even pre-embryonal memories merely by suggestion, without the use of hypnosis or drugs.

Now it may be seriously maintained that in spite of the immature state of the C.N.S. at birth, true and lasting (though unconscious) memories of that event are possible, although I myself much doubt it, but I do not think many medical men and women could accept the possibility of the existence of memories of life in the ovary or testis before the union of ovum and sperm, or of events occurring in the outer world while the subject was still *in utero*. Ehrenwald believes that the emergence of such material is due to "telepathic leakage" from the therapist, and certainly it may be so at times, but I would myself suggest that more often the patient has obtained the material by telepathic transmission from his mother during the first two or three years of his life. Sandison's finding that some of his patients identified themselves with their mothers and described their own birth from her point of view does obviously lend support to this hypothesis.

(b) *Inherited Memories*

The next class in this group of phenomena is that of what appear to be inherited memories, that is, memories of events and situations from the earlier history of the race. One attempt to explain this has led to the hypothesis of a "racial unconscious", and another was based on a Lamarckian theory of the inheritance of acquired characteristics, which few people in the West now find tenable. It seems to me that the occurrence of these "memories" is actually due neither to inheritance nor to the existence of a racial unconscious, but to telepathic transmission from the mother's unconscious to her young children generation after generation.

Presumably any event of emotional importance in the mother's life would be apt to be transmitted to the children in this way. If the memory of this were later emotionally reinforced in the child either because it was well-fitted to symbolize some important emotional conflict in her unconscious, or because some similar emotionally-charged event occurred in her own life, then the

child would in turn transmit this memory telepathically to her children, and so on, whereas material which was not so reinforced would not be passed on and the memory of it would die out. In this way, unconscious myth-like "racial" memories would come into existence, without their innate inheritance or any inborn changes in the C.N.S.

(c) *Innate Knowledge*

The third class of phenomena I mentioned was that of what seems to be innate knowledge. Certain analysts, (e.g. Klein, 1932) state that young children appear to have an unconscious knowledge of sexual intercourse, of the existence of at least some of the internal female sex organs, of the penis, and of the fact that babies grow in the mother's abdomen. Money-Kyrle (1951, 1956), has suggested the following explanation of this. In his paper "The World of the Unconscious and the World of Commonsense" he says: "We confidently assume that the physiological concomitant of memory is a cerebral process conditioned by an acquired modification perhaps in synaptic resistance, of some complex pattern of neurones. But it is possible to imagine that similar modifications could arise as the result of mutations in germ cells and that these would tend either to die out or to spread through the species, according to their value to it. If so, the psychic concomitant of cerebral processes determined by heritable modifications of this kind could be mistaken for racial memory, when in fact it was the result not of the experience, but of the mutations of former members of the species. In other words, if such mutations have occurred and been selected, we could, for example, be born into the world with some capacity to 'recognize' the more important objects and situations we are likely to encounter without having inherited any 'memory' of them."

Ehrenwald's (1947) explanation of this material is, again, that it is due to "telepathic leakage" from the analyst herself.

It seems to me at least as likely as either of these that the young child's knowledge of such matters is in fact obtained telepathically from its mother. Granted the occurrence of extra-sensory perception, Money-Kyrle's hypothesis becomes unnecessary. These three suggestions are obviously not mutually exclusive, however, and it may well be that all of them are correct.

There is a slightly different type of occurrence which I think might also be classed here. In a few cases I have seen in my Child Guidance work, children adopted in their third or fourth year from orphanages in which they had lived from two weeks old have produced fantasies of having watched sexual intercourse at some time during those first three years. I am now suggesting that this material may in fact have been obtained by extra-sensory perception from some mother-figure in the orphanage. I am of course aware that these children may have witnessed their adoptive parents' intercourse even when this is stated to have been impossible, and later have referred it back to the earlier period, but I should mention that in two of my cases the adoptive father had either died or deserted his wife within a few months of the patient's adoption.

(d) *Response to the Unconscious Feelings of Others*

My last class of phenomena in this group is that of the unmistakable response of young children to the unconscious emotional attitudes of the members of their family group, especially at first to their mothers. Anyone who has had to deal with emotionally disturbed, or indeed normal, children

cannot fail to have observed such responses, above all to unconscious rejection or hostility. All I wish to do here is to stress that it is difficult to account satisfactorily for an infant's awareness of its mother's *unconscious* mental content except by the hypothesis of telepathic communication between the two. This point is very well brought out by Ehrenwald in *New Dimensions in Deep Analysis*, and I can add nothing to what he says there.

Allied to the foregoing is the well-known fact that children who are believed to be unaware of being adopted nevertheless often show marked resentment of their adoptive mothers. There is no doubt that many of these children have in fact overheard references to the subject, or have been told by neighbours or adoptive siblings that they "aren't really" the mother's. With others, however, it does appear impossible for them to have learned the true position by the ordinary conscious channels. Even so, the child's resentment may obviously simply result from the adoptive parents' own attitude. There nevertheless remain cases in which the most probable explanation seems to be that the resentment is due to unconscious, telepathically-obtained knowledge that the adoptive mother did not in fact bear or breast-feed the child, and to all the train of fantasies to which such knowledge may give rise.

WHAT FOLLOWS FROM THE ABOVE?

If these suggestions are correct, then I think several interesting deductions can be made from them, of which I shall mention two.

(a) *Infantile Amnesia*

Firstly, if a free flow from the mother's mind to that of her young child does in fact normally take place, then a subsequent development of amnesia for these first few years of life would obviously be necessary. It is clear from some of the examples in the literature which I have given above that the recipient cannot afterwards distinguish between his own memories and those he has, so to speak, "picked up" from his mother, and he would therefore come to regard her experiences as his own (as indeed two of Sandison's cases did). If this material were not later forgotten, it would obviously result in much intellectual and emotional confusion and raise difficult problems concerning his own identity (as is also borne out by Sandison's account). It seems possible to suggest therefore that this is an important reason for the occurrence of the normal period of infantile amnesia. In this connection I might just mention Ehrenwald's (1947) hypothesis that the schizophrenic at one stage returns to a condition resembling the "open" infantile state with regard to the telepathic influx of heteropsychic material. As far as I am aware, however, the schizophrenic does not show that receptive sensitivity to a single individual which is apparent in the young child.

(b) *Importance of a Single Mother-figure*

Secondly, this extra-sensory perception by the child of much of the mother's mental content would explain the extreme importance for his satisfactory psychological development of the continuous presence of one single mother-figure during his early years.* One can imagine that the sudden appearance of a "mother" with a completely different mental content and a different picture of the infant would inevitably result in emotional shock and great psychological confusion in the young child. The fact that telepathy functions

* See Bowlby's (1951) Report to the World Health Organization.

independently of space would presumably mean that the child continued to receive at least some material from his first mother-figure for a time, and this would add to his confusion and resentment, so that one cannot wonder that such an experience gives rise to serious emotional maladjustment.

I referred above to the young child's "receptive sensitivity" to telepathically-conveyed material from a single person, obviously that is, from the biologically most important one, and therefore from his mother-figure. I presume that this telepathic "tuning in" must be achieved by emotional facilitation of reception from the possessor of the feeding breast (or its substitute), with inhibition or repression of material coming from other sources. When the child turns emotionally to the father, then presumably he develops a similar receptive sensitivity to him.

If a baby is deprived of his mother before he is old enough to perceive and conceive of her and of himself as whole persons and is placed in an institution where he is cared for by several different women in rapid succession, his psychological world must become completely chaotic. It is obvious that from the point of view of his extra-sensory perceptions, that world simply ceases to make sense, quite apart from the question of his emotional starvation. The child who has never had a single mother-figure after the critical age turns away from the outer world altogether, and we get the terrible pictures seen in Madame Roudinesco's film *Monique*, for example—pictures of children believed to be not only mentally defective but deaf and blind as well, who proved after psychotherapy to be physically and intellectually normal.

CONCLUSION

Ehrenwald (1954) says: "we must assume that there is a wellnigh unlimited two-way flow of mental content passing between parent and child", and again, "at this stage" (i.e. the pre-verbal), "telepathy serves a compelling biological need and represents a functional link between mother and child *here and now*, comparable to the function of instinct which, according to current concepts, forms the connecting link between successive generations in the longitudinal section of our racial history".

Hence, however fanciful my suggestions in the earlier part of this paper may appear to those not convinced of the reality of extra-sensory perception, or of however little practical use, I think no one will deny that if telepathy does occur and if it plays the role in early childhood which I have here described, its importance would be hard to over-estimate.

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SEDATION THRESHOLD, PERSONALITY, AND THE THEORY OF NEUROSIS

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INTRODUCTION

FOR many years it has been observed that individuals differ in their tolerance of depressant drugs. In everyday life differential susceptibility to the effects of alcohol is that most commonly observed and this fact led to McDougall's early theorizing (1929) about drug tolerance and personality. Also at this time Pavlov, in dogs, recorded differences in drug sensitivity in his various temperamental types. However, the first attempt to measure individual differences in drug tolerance was made by Shagass (1954), who proposed the concept of "sedation threshold". This was defined in terms of the amount of sodium amytal required to bring about certain behavioural and other changes in the individual, the threshold itself lying somewhere between the state of complete wakefulness and that of complete sedation. Two methods of determining the threshold were employed by Shagass. First, the point of onset of slurred speech gave an approximate estimate of its position. Secondly, a more accurate determination was made by means of EEG changes, specifically the point at which inflexion occurs in the amplitude curve of induced fast frontal activity.

In his original paper (op. cit.) Shagass reports that the sedation threshold correlates positively and significantly with ratings of tension in psychoneurotics. Later, Shagass and Naiman confirmed a revised hypothesis that sedation threshold was correlated with the level of manifest anxiety, rather than tension, this relationship being shown to hold in both normals (1955) and neurotics (1956). In the latter paper the authors also report the ability of the sedation threshold to discriminate between various groups of diagnosed neurotics, anxiety states having high and hysterics low thresholds, with mixed neuroses intermediate. This finding was later confirmed on a much larger group by Shagass and Jones (1958), the respectively high and low thresholds of anxiety states and hysterics being explained partly by the different levels of manifest anxiety found in these two classes of neurotic. Finally, Shagass and Kerenyi (1958) report that, in addition to its relationship with anxiety, sedation threshold is also correlated with introversion, the significance of the previous results being considered in terms of a personality syndrome of obsessionality-hysteria.

These findings corroborate a simultaneous but independent prediction by Eysenck (1955) that hysterics, being characterized by higher levels of cortical

inhibition than anxiety states, should respond more quickly to depressant drugs, which he has suggested (1957a) are inhibiting in nature. The discovery of a measurable threshold of sedation may be said, therefore, to have had important implications, both for the practical problem of diagnosis and treatment in psychiatry, as well as for the general theory of neurosis. Unfortunately, however, although recently a Danish worker, Nymgaard, has reported (1959) positive findings using EEG methods, attempts by workers in this country to duplicate Shagass's results have rarely been successful.

Eysenck (1957b), for example, reports difficulty in corroborating the findings on sedation threshold. Similarly, Ackner and Pampiglione (1958) found that in at least two-thirds of their cases it was difficult, or even impossible, to define a threshold, in terms either of slurred speech or of EEG changes. In those cases where a measure was determined no relationship with rated anxiety was found, while the mean sedation thresholds of anxiety states and hysterics were identical. Following an attempt to assess the objectivity of Shagass's methods, Thorpe and Barker (1957) conclude that the onset of slurred speech is quite unsatisfactory as an indicator of the sedation threshold. More successful was Laverty (1958), who was able to discriminate extraverted and introverted neurotics and normals and also demonstrated a slight increase in extraversion under the effects of sodium amytal. At the same time he reports that there was difficulty in many cases in assessing the sedation threshold from slurred speech.

It is clear then that, although the concept of sedation threshold may be regarded as an important one, an alternative method of measuring such individual differences in drug tolerance is desirable, if it is to be considered a useful tool for diagnostic and research purposes. The aim, therefore, at the beginning of the investigation reported here was to develop a method of measuring sedation threshold which was less subjective than the slurred speech index, but which could, unlike EEG methods, be easily administered and scored. Having done so, a number of important issues arose.

The first clearly relates to the ability of the measure to discriminate between groups of diagnosed neurotics. It is probable, for example, that the failure of Ackner and Pampiglione (*op. cit.*) to find differences between anxiety states and hysterics was due, rather to the uncertain nature of their sedation threshold measure, than to the lack of a real difference between these two groups. A more reliable index would be expected to confirm the findings of Shagass that the sedation threshold is low in hysterics and high in anxiety states or, as we shall call them here, dysthymics. Normals would be expected to have thresholds falling between those of the two neurotic groups.

The second problem concerns the relation of the sedation threshold to the general personality traits underlying dysthymia and hysteria. As already noted, both anxiety and introversion have been considered in this respect. According to Eysenck's original analysis of personality (1953) extraversion-introversion is the main dimension differentiating hysterics and dysthymics. It should follow, therefore, from his later predictions (1957a) with regard to the effect of depressant drugs, and, of course, the work of Shagass and Kerenyi (*op. cit.*), that sedation threshold will correlate negatively with a measure of extraversion. At the same time, the findings of Sigal, Star and Franks (1958), and later of Claridge (1960a), have indicated that hysterics are not as extreme on extraversion as was at first thought and, in addition, tend to have lower scores than dysthymics on a neuroticism scale. Since this is clearly relevant to the link which has been suggested between anxiety and sedation threshold, it might be expected

that the latter would correlate positively with a measure of neuroticism as well as, of course, with a measure of manifest anxiety itself. Indeed, in making these predictions it was hoped that the correlations in this part of the study would help to elucidate the personality determinants of and, therefore, the psychophysiological processes underlying, sedation threshold.

This point serves to introduce the third issue, which concerns the significance that the concept of sedation threshold undoubtedly has for contemporary psychological theories of behaviour, particularly recent activation or arousal theories of drive (Hebb, 1955; Malmö, 1959), as well as Eysenck's postulate of a link between central inhibition and dysthymia-hysteria. The relation of the arousal concept to Eysenck's theory of neurosis has been considered in a previous paper (Claridge, 1960a), where, after an intensive investigation of the behaviour of neurotics, it was concluded that differences between dysthymics and hysterics in drive level probably accounted for some of the inter-group differences in performance on perceptual and motor tests. A factor analysis of the data from this study did in fact reveal a factor recognizable as one of drive and having loadings on a neuroticism scale.

More recently (Claridge, to appear), this hypothesis has been confirmed and a modification to Eysenck's theory suggested, to the effect that there may be in dysthymics and hysterics an effective shift in the excitation-inhibition balance assumed to underly the dimension of introversion-extraversion. The hypothesis proposed is that the excitation-inhibition balance and the level of arousal are linked in such a way that upward or downward changes in the latter will be reflected in a parallel shift in the excitation-inhibition balance. Thus, it is further hypothesized that in hysteria a decrease in arousal levels occurs resulting, other things being equal, in a more rapid growth of inhibitory processes than would be predictable from the hysteric's position on the introversion-extraversion continuum. A corresponding delay in the growth of inhibition would be expected from the heightened arousal level which it is proposed occurs in dysthymia.

In the previous studies quoted above no independent measure of arousal was forthcoming, although three sources of evidence were considered to point to anxiety as an important determinant of arousal differences in neurotics. These were (a) the finding, noted above, that hysterics and dysthymics differ in "neuroticism", together with the traditionally held view that the hysteric, in contrast to the dysthymic's heightened manifest anxiety, is characterized by the so-called "belle indifference" resulting from his "conversion" of anxiety; (b) the link found between performance, arousal level, and measures of the autonomic activity associated with anxiety (Malmö, 1957); and (c) the finding, such as that of van der Merwe (1948) that hysterics and dysthymics differ on such measures.

Clearly relevant in this context is the likelihood of a positive relationship between anxiety and sedation threshold, since it suggests that the latter may be a good index of arousal level. If so, it would be expected to bear systematic relationships with those aspects of performance on objective tests which may be considered to reflect the level of behavioural arousal or drive. Additionally, since it has been suggested that the excitation-inhibition balance, and therefore the relative proneness to inhibition, is partially dependent on arousal level, it would be anticipated that sedation threshold would tend to be negatively correlated with measures of inhibition.

The aim, therefore, of the study reported here was fourfold and may be summarized as follows: (1) to develop a simple, reliable index of the sedation

threshold; (2) to determine the extent to which this measure differentiated hysterics, normals, and dysthymics; (3) to determine the relationships between the sedation threshold and various measures of personality; (4) to investigate the relationship between the sedation threshold and a number of measures from objective performance tests, in order to clarify some of the issues arising from the postulate that excitation-inhibition is an underlying concomitant of dysthymia-hysteria.

SELECTION AND DESCRIPTION OF SUBJECTS

For the two patient groups consecutive untreated neurotic admissions between September and December, 1959 were selected where the psychiatrist in charge of the case could make a definite diagnosis of anxiety state or hysteria. Cases of immaturity were not included. Patients with evidence of brain damage, those with addiction to drugs or alcohol, and those subsequently shown to be psychotic were rejected. In each of the neurotic groups there were fourteen male and two female patients.

The normal control group consisted of sixteen volunteers, of whom fifteen were male and one female. All were engaged on various duties in the hospital, including that of nursing orderly, clerk, storeman, and laboratory technician.

The means for the three groups on age, weight, and Matrices I.Q. are shown respectively in Tables I, II and III. Only on age was there an overall

TABLE I
Mean Age (in Years) for Each Group

				Dysthymics	Normals	Hysterics
Mean	..	..	..	27.91	23.67	23.78
S.D.	..	..	..	5.987	4.559	4.916

F-ratio: 3.239, $p < 0.05$.

t-tests: Dysthymics v. Hysterics, 2.176, $p < 0.05$; Dysthymics v. Normals, 2.234, $p < 0.05$; Hysterics v. Normals, 0.058, N.S.

TABLE II
Mean Weight (in Pounds) for Each Group

				Dysthymics	Normals	Hysterics
Mean	..	..	..	149.88	142.56	155.50
S.D.	..	..	..	13.042	20.860	21.943

F-ratio: 1.742, N.S.

TABLE III
Mean Matrices I.Q. for Each Group

				Dysthymics	Normals	Hysterics
Mean	..	..	..	111.31	113.25	106.25
S.D.	..	..	..	14.358	10.542	9.093

F-ratio: 1.472, N.S.

significant difference between the groups, dysthymics being just significantly older than both hysterics and normals. although the latter two groups did not differ on this variable. The tendency for dysthymic reactions to present later than hysterical syndromes is thus reflected in the present sample, but this was not considered important, since Shagass and Jones (op. cit.) have shown that there is no correlation between sedation threshold and age.

EXPERIMENTAL PROCEDURE

Sedation Threshold

The sedation threshold was assessed in terms of the effect of sodium amytal on a simple task of attention. The stimulus material consisted of a tape-recording of random digits, relayed to the subject through earphones. While receiving a continuous intravenous infusion of sodium amytal at the rate of 0.1 G/min., the subject was required to respond by doubling the digits, which occurred regularly at intervals of two seconds.

The digits were grouped on a score sheet into blocks of five and the errors recorded were then plotted against blocks, giving graphs of the form shown in Figure 1. The threshold was taken as the point midway between the last two blocks with less than 50 per cent. error and the first two blocks in which errors exceeded 50 per cent. In the majority of cases these blocks were consecutive. The amount of drug administered at this point was determined from a chart relating blocks to drug received and this dosage corrected for the weight of the patient, giving the threshold in terms of mg./Kg.

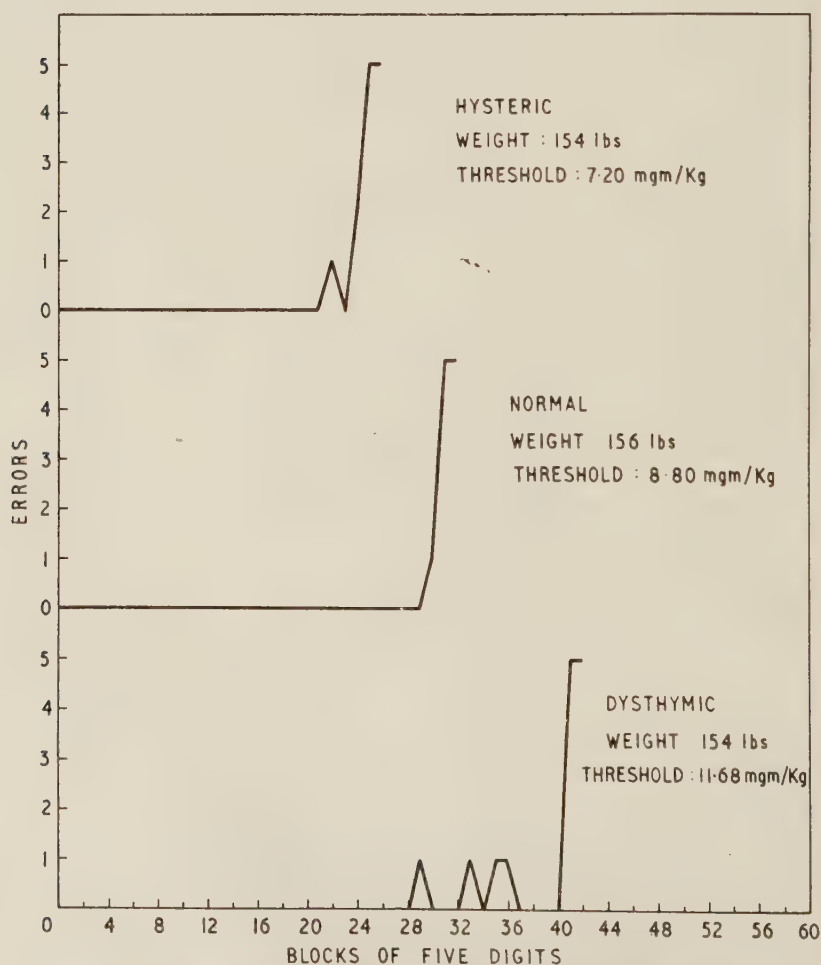


FIG. 1.—Typical sedation threshold curves: one subject from each group.

The onset of slurred speech was not related to the threshold as measured in this way, though other behavioural changes consistently preceded the end-point. This was heralded by a raising of the voice with increase of muscle tension, soon to be followed by relaxation and noticeable slowing of the reaction time, leading to perseveration before the end-point was reached.

Psychological Tests

In order to obtain estimates of the relevant personality traits two questionnaires were administered to each subject. These were the Maudsley Personality Inventory (MPI), giving estimates of extraversion (E-scale score) and neuroticism (N-scale score), and the Taylor Manifest Anxiety Scale (MAS). Two objective performance tests were also administered.

The first was a five-choice serial reaction time task. It consisted of a display panel set at 15 degrees from the vertical and containing five lights placed two inches apart in a horizontal row. In front of each light and in the horizontal plane was a key five inches long and approximately one inch wide. In operation the subject is required to press the key corresponding to the light which is lit at any one time, thus extinguishing it and illuminating another light to which a further response is made and so on. The order in which the lights were illuminated was a random one over a series of 50, except that no light appeared twice in succession. The subject's responses were registered on a simple counter, the score being recorded for each minute of the work period. The schedule followed in the present study consisted of a period of ten minutes' continuous performance, followed by a rest of five minutes and a further period of practice for one minute.

A consistent pattern of performance shown by most subjects on this test (Venables, 1959) is a gradual decline in performance level during the first five minutes, then an increase in speed during the second five minutes of practice. Following the rest the usual reminiscence effect appears, in the form of an abrupt rise in performance level. The four major measures which can usefully be extracted from the test are those of starting level, rate of initial fall-off, total number of errors, and reminiscence change. The underlying variables which are probably reflected in these measures have been outlined elsewhere (Claridge, 1960b) and will be considered only briefly here.

It has been suggested that starting level reflects the drive or arousal level of the subject and, as such, has been shown (Claridge, to appear) to differentiate hysterics and dysthymics, the latter performing at a significantly faster rate than the former. In the present experiment it would be predicted, therefore, that this measure would correlate positively with sedation threshold, if, as we have suggested, the latter is an index of arousal level.

Changes in performance subsequent to the beginning of the test may be said to be due to the onset of inhibitory processes, the accumulation of inhibition being expected, for instance, partly to account for the initial fall-off in level which occurs. Also contributing to this decline is the onset of gaps in performance, which have been shown (Broadbent, 1958) to occur in this type of task. The approach taken by the present authors is that these gaps serve partly to dissipate previously accumulated inhibition and, therefore, themselves serve as an index of inhibition. A reliable overall measure of such gaps has been found to be errors or incorrect responses on the test, the assumption being that, even though a response is made, inhibition *centrally* accumulated will be partly dissipated in the same way as during the less frequent gaps which occur without a simultaneous error. Any inhibition undissipated at the end of the test should be reflected in the reminiscence measure.

In view of the hypothesis presented earlier relating arousal to excitation-inhibition, it would be expected that sedation threshold would correlate negatively with these three measures of inhibition, viz. rate of fall-off, total errors, and reminiscence. A complicating feature, however, is that, in terms of the *absolute* degree of inhibition induced by performance, the differential response rate associated with different arousal levels may tend to cancel out any effect which changes in arousal level may have on the rate of inhibitory growth *per unit response*. Thus, in the paper previously cited (Claridge, to appear) hysterics tended to show *less* fall-off in performance than dysthymics, while the two groups did not differ on either reminiscence or errors. By partialling out the effect of differential performance levels results more in line with expectation were forthcoming. It may be anticipated, therefore, that the present hypothesis with regard to sedation threshold and inhibition will have to be interpreted with these findings in mind.

The second performance test used was the Archimedes Spiral. Here the subject is asked to fixate a rotating spiral for a given length of time and to report on the duration of the subsequent after-image which occurs when the spiral has ceased. The direction of rotation experienced as the after-image is always opposite to that obtaining during the stimulation period. In the present study a single-throw 180 degree spiral was used, four trials being given. In each trial the spiral was rotated for one minute, alternately clockwise and anti-clockwise, with a rest of one minute between trials. The mean of the four scores thus obtained was taken as a measure of the subject's performance on the test.

The processes underlying the spiral after-effect are unclear, although Eysenck (1957b) has argued that its length is inversely proportional to the amount of inhibition produced by the persistence of excitation after the spiral has ceased rotating. A similar explanation, leading to the same predictions, but taking into account the inhibition produced during the stimulation period itself, was proposed by Claridge (1960a), who was able to show that dysthymics have significantly longer after-images than hysterics and, further, that the spiral after-effect was positively loaded on a factor of drive. Despite the lack of certainty about the underlying processes involved, it seems reasonable to assume that this phenomenon is in some way related to the balance between excitation and inhibition obtaining at the end of the period of stimulation, whether it is held that the after-effect itself is a persistence of excitation or a reflection of the inhibition existing at this point. It was possible to predict in the present experiment, therefore, that sedation threshold would be positively correlated with the spiral after-effect.

RESULTS

Group Differences in Sedation Threshold

As anticipated, there were marked differences between the three groups on the sedation threshold measure. It can be seen from Table IV that the mean

TABLE IV
Mean Sedation Threshold (in mg./Kg.) for Each Group

	Dysthymics	Normals	Hysterics
Mean	10.18	7.86	6.43
S.D.	1.608	1.313	1.774

F-ratio: 21.837, $p < 0.001$.

t-tests: Dysthymics v. Hysterics, 6.544, $p < 0.001$; Dysthymics v. Normals, 4.049, $p < 0.001$; Hysterics v. Normals, 2.496, $p < 0.02$.

threshold for dysthymics was significantly higher than that of either normals or hysterics, while the latter two groups were differentiated at a lower, but still very acceptable, level of confidence. Typical sedation threshold curves are shown in Figure 1, where are plotted, for comparison, the results for three subjects of equivalent weight, one subject being from each group.

One aspect of the results which should be noted is the general tendency for the thresholds, as measured in this study, to be higher than those reported by Shagass and his co-workers. EEG changes would, of course, be expected to precede changes at the behavioural level and, in addition, in the method used here it is probable that the task had a slight alerting effect on the subject. Nevertheless, it is clear that the two methods produce comparable results.

Sedation Threshold and Personality

In Tables V, VI and VII are shown the mean scores for each group on the MAS and the E and N scales of the MPI. Product moment correlations

TABLE V
Mean M.A.S. Score for Each Group

				Dysthymics	Normals	Hysterics
Mean	..	..	..	17.00	6.25	13.69
S.D.	..	..	..	3.774	3.699	5.860

F-ratio: 21.903, $p < 0.001$.

t-tests: Dysthymics v. Hysterics, 1.990, $p < 0.1$; Dysthymics v. Normals, 6.464, $p < 0.001$; Hysterics v. Normals, 4.474, $p < 0.001$.

TABLE VI
Mean E-scale (M.P.I.) Score for Each Group

				Dysthymics	Normals	Hysterics
Mean	..	..	..	18.31	31.50	24.62
S.D.	..	..	..	8.169	7.575	8.366

F-ratio: 10.120, $p < 0.001$.

t-tests: Dysthymics v. Hysterics, 2.152, $p < 0.05$; Dysthymics v. Normals, 4.499, $p < 0.001$; Hysterics v. Normals, 2.346, $p < 0.05$.

TABLE VII
Mean N-scale (M.P.I.) Score for Each Group

				Dysthymics	Normals	Hysterics
Mean	..	..	..	36.62	19.12	31.19
S.D.	..	..	..	7.631	8.392	11.092

F-ratio: 14.354, $p < 0.001$.

t-tests: Dysthymics v. Hysterics, 1.624, N.S.; Dysthymics v. Normals, 5.235, $p < 0.001$; Hysterics v. Normals, 3.610, $p < 0.001$.

between sedation threshold and these three measures were calculated over the total group of 48 subjects. The correlation between sedation threshold and the E-scale was -0.271 , which was not significant. Both the N-scale and MAS were found to correlate significantly with sedation threshold, the values for r being $+0.355$ ($p < 0.05$) and $+0.383$ ($p < 0.01$) respectively. It is interesting to note, however, that within the normal group only a significant correlation was present between extraversion and sedation threshold, the value for r here being -0.524 ($p < 0.05$).

While the predicted relationship with extraversion is thus partly confirmed, the results for the total group indicate that sedation threshold is associated more

directly with the level of manifest anxiety and general neuroticism than with the personality dimension of introversion-extraversion. This change in emphasis away from extraversion is perhaps further evidence, similar to that quoted earlier, of the over-riding role played by factors associated specifically with neurosis when abnormal groups are included in the study of extraversion. That the relationship between sedation threshold and the processes underlying anxiety are not, however, completely uncovered by the present findings is suggested by the fact that, despite the overall correlations with both N and MAS, the hysteric group, while having higher scores than normals on both questionnaires, emerge with significantly lower thresholds. This is presumably due to the fact that the questionnaire measures do not entirely reflect the changes occurring at the onset of neurotic breakdown and in this respect the need for objective measurement of the autonomic activity involved may be emphasized. Nevertheless, there seems to be sufficient evidence in the present findings to allow us to accept the hypothesis that sedation threshold measures differences in arousal level arising as a result of variations in the degree of manifest anxiety.

Performance Tests and Sedation Threshold

(a) *Serial reaction time.* As pointed out previously, four measures from this test were investigated, viz. starting level, fall-off during the first five minutes, total number of errors, and reminiscence change. The first two of these measures were obtained by calculating the coefficients of linear regression on each subject's scores during the first five minutes (trials) of the test. This gave two measures, the coefficient "b" representing starting level, and the coefficient "a" representing mean change per trial or rate of fall-off*. The group means for each of the four measures taken from the five-choice test are shown in Table VIII.

The correlation between sedation threshold and the "b" coefficient was found to be $+0.366$, which is significant at the 0.05 level (d.f. 46). Thus, the assumption that starting level on this test reflects the general drive or arousal of the subject was justified, in so far as sedation threshold may be said, from our conclusions in the previous section, to be an index of this variable.

In view of this correlation it was apparent that the analysis of the relationship between sedation threshold and measures of inhibition was to be a complex one, since, as pointed out earlier, it was likely that the high rates of response associated with high arousal had led to greater absolute amounts of inhibition being accumulated at some stages in the test, even though, as hypothesized, the rate of inhibitory growth, or amount produced per response, may be reduced under heightened arousal.

It was not unexpected, therefore, that the correlation between the "a" coefficient and sedation threshold was negative, the value for r being -0.173 (N.S.). In order to investigate the relationship between sedation threshold and *relative* fall-off the effect of differences in starting level was partialled out, the correlation between "a" and "b" being -0.481 ($p < 0.01$). The resulting partial r had a value, however, of exactly zero, thus not confirming, for this sample, the tendency previously reported (Claridge, to appear), for the more poorly aroused hysterics to show relatively greater fall-off than dysthymics. There were two possible explanations for this lack of relationship between

* To avoid confusion it should be pointed out that the more negative the value for "a" the greater the degree of fall-off. Negative correlations between "a" and other variables should, therefore, be interpreted with this in mind.

TABLE VIII
Five-choice Test: Mean Score on Four Measures /or Each Group

	Dysthymics	Normals	Hysterics
(i) Coefficient "b" (Starting Level)			
Mean	90·14	82·34	77·51
S.D.	15·412	11·331	12·499
F-ratio: 3·530, $p<0\cdot02$.			
t-tests: Dysthymics v. Hysterics, 2·632, $p<0\cdot02$; Dysthymics v. Normals, 1·625, N.S.; Hysterics v. Normals, 1·007, N.S.			
(ii) Coefficient "a" (Rate of Fall-off)			
Mean	-1·22	-0·12	-0·23
S.D.	1·954	1·451	1·713
F-ratio: 1·993, N.S.			
(iii) Reminiscence			
Mean	13·00	13·88	12·94
S.D.	9·434	8·901	9·473
F-ratio: 0·048, N.S.			
(iv) Errors			
Mean	11·12	8·63	19·88
S.D.	10·705	8·748	20·524
F-ratio: 2·563, N.S.			

sedation threshold and relative fall-off: either we were incorrect in our hypothesis that arousal level and rate of inhibitory growth are inversely related; or some other factor was operating to cancel out the expected effect.

The reminiscence measure was therefore examined. The correlation between reminiscence and sedation threshold proved to be $-0\cdot135$, a lack of correlation which is reflected in the mean reminiscence scores for the three groups (see Table VIII). It was apparent from this that, although the more highly aroused subjects performed at a significantly faster rate, the absolute amount of inhibition accumulated during the test was identical with that of the slower, less aroused subjects. In order for this to occur the amount of inhibition produced per unit response must have been greater in the poorly than in the highly aroused subjects, thus confirming the original hypothesis.

How then do we explain the negative findings on fall-off, which seem somewhat paradoxical? Reference to Figure 2 suggests a likely explanation.

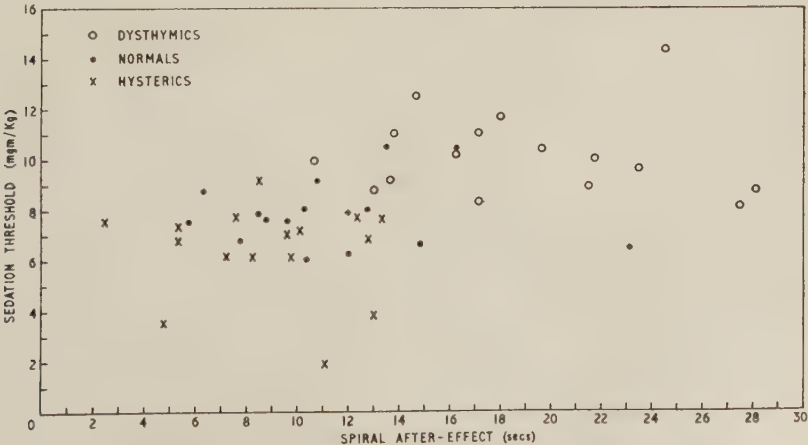


FIG. 2.—Serial reaction time: mean performance curve for 48 subjects.

Seen clearly in this figure is the abrupt initial decline characteristic of the test. By the second half of practice this decline has become minimal, although the increase in speed expected at this point fails to appear in the present sample. It seems possible that all subjects proceed from the beginning of the test towards a stabilization of the balance between excitation and inhibition, the point of equilibrium occurring after about five or six minutes. The rate at which this proceeds is determined principally by the absolute number of responses made at the beginning of the task when inhibition is negligible; hence the correlation between "a" and "b" coefficients. Since high arousal prompts the subject to start at a higher level, the absolute amount of inhibition accumulated in the earlier stages of the test will probably be greater than in poorly aroused subjects and hence have a greater decremental effect on performance, i.e. produce greater fall-off. As this greater amount of inhibition begins to reduce response rate so the absolute amount of inhibition produced will decrease until a point is reached where both high and low arousal subjects are accumulating the same absolute amounts of inhibition. The response rate during the test is thus modulated in order to keep inhibition at a minimum level appropriate to the degree of arousal present. Since, as seems to be the case, heightened arousal reduces the amount of inhibition produced per response, this allows the subject to continue performing during the later stages at a higher level without producing by the end of the test a greater amount of inhibition to be dissipated in reminiscence.

One of the factors which allows inhibition to be kept at a minimum in the way proposed is the occurrence of gaps or errors in performance, which we have suggested serve the purpose of partly dissipating inhibition. The analysis of performance gaps is perhaps usefully considered in terms of Kimble's "critical level" principle. Briefly, he has suggested (1949) that inhibition builds up until it reaches the level of positive drive, or critical level. At this point a short pause occurs so that inhibition can dissipate sufficiently to allow correct performance to continue. Re-interpreting this analysis and applying it to the present data, it would be expected that a combination of low critical level (arousal) and the faster inhibitory growth rate associated with it would result in more frequent errors in poorly aroused subjects than in those with high arousal levels. This was confirmed by a significant correlation between sedation threshold and the measure of total errors, the value for r being -0.395 ($p < 0.01$).

The weight of evidence from this part of the study undoubtedly points to a confirmation of the hypothesis that there is a relationship between arousal and central excitation-inhibition, such that the relative proneness to inhibition is reduced where the level of arousal is high, and vice versa. One fact which does emerge, however, is the difficulty of obtaining adequate measures of inhibition. By using a self-paced task we unwittingly allowed the subjects to adjust their response rates so as to minimize inhibition, and so cancel out individual differences on all measures of this variable, except, significantly, that one which was itself involved in the maintenance of the excitation-inhibition balance. That there should have been a tendency in all subjects to maintain equilibrium in this way is not surprising, in view of the frequent operation of homeostatic processes at other levels of behaviour. Indeed, homeostasis is inherent in the concept of a balance, within the nervous system, between excitatory and inhibitory mechanisms.

(b) *Archimedes spiral*. In Table IX is shown the mean spiral after-effect for each group, together with significance levels for the inter-group differences.

TABLE IX
Mean Spiral After-effect (in Seconds) /or Each Group

	Dysthymics			Normals			Hysterics		
Mean	..	..	..	18.79	11.41		8.85		
S.D.	..	..	..	5.093	4.125		3.767		

F-ratio: 22.576, $p < 0.001$.
t-tests: Dysthymics v. Hysterics, 6.476, $p < 0.001$; Dysthymics v. Normals, 4.808, $p < 0.001$; Hysterics v. Normals, 1.668, N.S.

A relatively high correlation was found between the spiral after-effect measure and sedation threshold, r being $+0.456$ which, for 48 subjects, is significantly beyond the 0.01 level of confidence. This result is also shown graphically in Figure 3, where it can be seen that there is a clear separation, without overlap, between the two neurotic groups, the normals falling in a roughly intermediate position.



FIG. 3.—Sedation threshold and spiral after-effect.

We have already considered the two alternative explanations of the spiral after-effect, viz. that it is either a persistence of excitation after the spiral has ceased rotating, or that it reflects the amount of inhibition existing at the end of the stimulation period. The first is the simpler explanation, since it accounts directly for the greater after-effect shown by subjects with high arousal. However, it seems more likely that the spiral after-image arises as a result of inhibition generated during the prior stimulation. It is of interest, therefore, to reconsider, in the light of the theoretical approach developed here, the probable course of events occurring during performance on the spiral test.

Stimulation with the rotating spiral clearly serves, in effect, to disturb the balance of excitation-inhibition. Simultaneously with this increased excitation, inhibition is presumably generated, this tending to oppose and therefore to reduce the excitation level. Since the initial disturbance should be greater in

highly aroused subjects and since, as shown in the previous section, the tendency to produce the opposing inhibition will be correspondingly reduced, the total amount of excitation developed throughout the stimulation period will be higher in these subjects than in those with low initial arousal. In keeping with this the total *absolute* amount of inhibition induced, and therefore the after-effect, will be greater in highly aroused than in poorly aroused subjects. To put the argument more crudely, the greater the absolute disturbance of equilibrium the greater will be the time required to recover.

It is apparent from this that, although the amount of physical stimulation on the spiral test is identical for all subjects, the same assumption cannot be made in the case of the central effects of this stimulation which are critically related to the balance between excitation and inhibition, and hence arousal level, in much the same way as was found to be the case on the serial reaction time test discussed previously.

DISCUSSION

In so far as on sedation threshold the three groups in this study were clearly differentiated in the predicted direction, the results may be said to support Eysenck's theory of dysthymia-hysteria. Thus, the greater tolerance of sodium amytal found in dysthymics links his postulate that depressant drugs are inhibiting in nature with the hypothesis that the excitation-inhibition balance is weighted towards the positive (excitatory) side in anxiety states, while the opposite is true of hysterics.

Not entirely consistent, however, with this theory, but supporting previous results quoted earlier, is the finding that, while within the normal group the sedation threshold is predictable from the degree of extraversion present, this relationship fails to hold in the neurotic group; where manifest anxiety appears to be a more important determinant of the susceptibility to the effects of barbiturates. This, together with the findings from the objective performance tests, supports the hypothesis proposed at the beginning of this paper that a shift occurs in the excitation-inhibition balance of dysthymics and hysterics.

We have already suggested that this shift is attributable to changes in neurotics in the level of arousal and it is appropriate, therefore, to consider at this point the implication that arousal theory undoubtedly has for the problems under discussion. It is particularly relevant in the present context since neurophysiological evidence clearly relates arousal to anxiety and to differential susceptibility to depressant drugs.

Hebb (1955), for example, relates arousal to the activity of the ascending reticular formation and it is known that heightened activity of the mesencephalic (adrenergic) component of this system is accompanied by both EEG and behavioural arousal (Bradley and Elkes, 1957). Its activation has been demonstrated in physiological drives (Dell, 1958) and can be inferred clinically from the raised plasma-adrenaline (Weil-Malherbe, 1955) and fast low voltage EEG patterns (Lindsley, 1951) found in dysthymics. Since barbiturate anaesthesia initially and most markedly affects the activity of the reticular formation (King, 1956; Arduini and Arduini, 1954; French *et al.*, 1953), increased activity of this system should be reflected in increased tolerance of sedation.

The neurophysiological evidence that relatively long-term changes in the state of arousal are feasible may be paralleled at the behavioural level by the finding of Shagass (1958) that a decrease in sedation threshold accompanies a

reduction in the anxiety symptoms of the dysthymic neurotic. Comparable increases in the thresholds of remitted hysterics appear not to have been reported, although an investigation of this would be of considerable interest. That such changes would occur seems feasible if the behavioural aspects of hysterical conversion of anxiety are taken in conjunction with the fact that both descending and ascending effects are present in reticulo-cortical relationships.

Clinical and experimental evidence, both psychological and physiological, thus supports the contention that a link may be possible between arousal theory and Eysenck's inhibition theory of personality. To attempt a detailed integration of these two approaches at the moment would involve going far beyond the available facts. Particularly necessary is a more thorough investigation, in both normals and neurotics, of how measures of arousal in terms of autonomic functioning are related to the sedation threshold. The possibility of such a relationship is considered by Gellhorn (1957) in his discussion of hypothalamic imbalance and cortical excitability; its relevance to the problem of dysthymia-hysteria, and introversion-extraversion, is suggested by van der Merwe's findings (*op. cit.*) that anxiety states tend towards sympathetic and hysterics towards parasympathetic predominance in their autonomic reactions.

For the present it seems useful to consider the excitation-inhibition balance proposed by Eysenck as the complex result of an interaction, on the one hand, between subcortical and cortical influences and, on the other hand, between, at each of these levels, positive excitatory effects and the negative opposing (inhibitory) effects which psychologists have found it necessary to postulate and which physiologists in recent years have been able to demonstrate at some levels of central nervous integration (e.g. at the cellular level as discussed by Eccles (1958)). The ascending activating effect of autonomically-linked arousal mechanisms is thus just one factor which may be thought of as influencing this excitation-inhibition balance* and therefore performance. By emphasizing the importance of some of the possible underlying processes associated with neuroticism, this approach helps to account for the discrepancies found in recent studies relating dysthymia-hysteria to the personality dimension of introversion-extraversion.

In conclusion, it is perhaps pertinent to return to the point from which this study started, namely the sedation threshold. The importance of the latter as a research tool has certainly been vindicated, since it has been possible to uncover by this technique individual differences in nervous functioning which are meaningfully related to both human performance and personality. Indeed, the results as a whole may be said to have underlined the fact, already recognized by Eysenck, that the interrelated fields of psychopharmacology and personality hold a key place in the search for the laws underlying not only human behaviour in general, but also its normal and abnormal variations.

SUMMARY

In this paper a new method of measuring the "sedation threshold" was described. Confirming previous work, sedation thresholds were found to be

* While in this paper emphasis has been laid on the positive relationship between efficiency of performance and arousal level, the authors are not unaware that at excessive arousal levels a reversal of this relationship may occur, giving rise to the U-shaped functions commented upon by a number of psychologists, including Duffy (1957), Malmö (1959) and Hebb (1955). This is quite consistent with the approach taken here if it is assumed that minimal inhibition may interfere with, rather than facilitate, performance on some tasks. This is particularly so on complex tasks, where U-shaped functions are most likely to appear, and where the inhibition of irrelevant stimuli may be essential for efficient performance.

significantly higher in dysthymics than in hysterics, while a normal control group had a mean threshold falling between those of the two neurotic groups. Correlations calculated over the total group indicated that sedation threshold was correlated significantly and positively with measures of manifest anxiety and general neuroticism. A significant correlation with extraversion was found only when the normal group was taken separately. It was suggested that sedation threshold measures differences in arousal level arising from variations in manifest anxiety.

The relationship was then examined between sedation threshold and performance on two objective tests: Archimedes spiral and a five-choice serial reaction time task. On the latter sedation threshold was correlated significantly with starting level and negatively with errors, while reminiscence was identical in both high and low arousal subjects. This indicated that, despite leading to a higher response rate, heightened arousal did not induce greater absolute amounts of inhibition but in fact reduced the growth rate of inhibition. A positive correlation between sedation threshold and the spiral after-effect was also reported.

A link was suggested between arousal theory and Eysenck's inhibition theory of personality, the differences between hysterics and dysthymics being explained in terms of a shift, due to changes in the state of arousal, in the excitation-inhibition balance underlying introversion-extraversion.

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SEVERE REACTIONS TO FENTAZIN IN MENTAL DEFICIENCY PRACTICE

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FENTAZIN—Perphenazine—is a phenothiazine derivative which has gained a considerable amount of popularity with psychiatrists employed in treating severe schizophrenia and chronic psychosis. At present, however, there would appear to be few reports of its use in mental deficiency practice.

The object of this paper is to describe two cases of severe reactions to Fentazin during its use at Balderton Hospital.

Case 1. The patient was a 15-year-old hyperactive, destructive idiot boy. He had been treated with short courses of various tranquillizers previously with no effect. In late June it was decided to try Fentazin and this was commenced with a daily dosage of 2 mg. oral t.d.s. Six days later the dose was increased to 2 mg. morning and noon and 4 mg. nocte. His mental condition improved somewhat. He became more manageable as regards toilet training and he began to speak—uttering individual words and short phrases—a thing he had never been known to do since his admission to hospital four months previously. Four days after the last increase in dosage his medication was increased to 4 mg. oral t.d.s. Ten days later due to a nursing mistake he was given 4 tablets (i.e. 8 mg. t.d.s.) and this was continued for 7 days prior to the onset of symptoms. During this time his behaviour was gradually improving in the ward so that he was not incontinent during the day at all throughout the last week.

Side-effects commenced suddenly following the mid-day dose of the drug. Firstly the nurse in charge of the ward noticed that the patient had become extremely pale. He refused to mix with the other patients and sat alone staring into space. This was followed by a tremor affecting both upper limbs that was Parkinsonian like in its characteristics. After approximately one hour his condition deteriorated. He developed a severe head retraction backwards and to the right which was associated with a marked spasm of the long spinal muscles. His gait became unsteady and attempts to walk forwards were accompanied by sideways movements to the right. The patient had little spontaneous activity at this time, but, on one occasion indicated that he would like a drink. On attempting to drink, however, it was found that he was quite unable to swallow and the fluid ran from his mouth. He became pale, cold, and shocked, temperature was subnormal and pulse rate remained at about 120 beats per minute. Blood pressure, pupillary reactions and reflexes appeared normal. There was some diminution of tone in the right arm and leg. Plantar responses remained flexor.

No further Fentazin was given. The patient remained in bed and was treated generally for shock. After 9 hours his symptoms began to disappear. The head retraction went and returned intermittently over a period before ceasing altogether. With its cessation the ability to swallow returned. After 24 hours all symptoms had ceased and the patient appeared to have returned to his former self.

Case 2. This was a 19-year-old boy with an I.Q. of 66, in good physical health, with a clinical picture of schizophrenia. He was placed on an oral dosage of Fentazin of 4 mg. t.d.s. He developed a reaction to the drug after 3 days on this dosage. He returned from work at 3.30 p.m. complaining that he could not hold his shoulder properly and that he felt unwell. On examination he was found to be sweating profusely though his temperature was normal. His pulse rate was about 120/minute and his right shoulder appeared to have dropped to a lower level compared with the left. There was a considerable rigidity of the shoulder muscles and of the muscles of the right side of his chest. His Fentazin was stopped and he was put to bed. Two hours later he was feeling better and his pulse rate had dropped to 110/minute. He ate his tea and following this one of the other boys gave him a bottle of "fizzy lemonade". He drank this off rather hurriedly about 6 p.m.

Thirty minutes later he suddenly collapsed. His pulse rate rose to over 140/minute. The sweating recurred much more severely and was accompanied by excessive salivation. The former was so severe that the bedclothes were wringing wet through to the mattress. At 6.45 p.m. he was looking extremely grey and shocked when he had a sudden onset of muscular

spasms. These commenced in his jaw muscles and passed downwards affecting his throat so that he became unable to swallow. He then suddenly went into opisthotonus which was complicated by severe torsional spasms rotating him first to one side, then to the other. His breathing became extremely irregular and due to his inability to swallow it became apparent that there was a grave danger of his drowning in his own excessive secretions of saliva. These were sucked clear and Atrophine gr. 1/100 given. Oxygen was administered throughout. The spasms ceased spontaneously after 10 minutes leaving the patient shocked and exhausted.

At 7.20 p.m. there was a recurrence of the muscular spasms as described above. This time the contractions lasted for 15 minutes and the patient was extremely cyanosed and distressed when they ceased. Five minutes later they recurred again, this time lasting for a period of three minutes.

At 7.55 p.m. there was a further short spasm lasting only 20 seconds, following this the patient fell into an exhausted kind of sleep. He gradually settled down and his pulse rate had fallen back to 120/minute with respiration at 20/minute by 8.15 p.m. At 8.30 p.m. the pulse rate again rose to 140/minute and was accompanied by a fresh series of muscular spasms during which respiration ceased but returned after 30 seconds. This bout of contractions lasted for five minutes. Following these the patient again fell asleep and slept for the rest of the night without further incident. His pulse rate fell gradually and by the morning he was bright and cheerful and appeared to have returned to his former self.

DISCUSSION

Severe reactions to Fentazin of a type similar to those above do not appear to have been described previously in defectives, though prominent extrapyramidal symptoms occurring during treatment of psychotics have been reported—1, 2 and 3. The characteristic thing about these reactions in the treatment of psychotics would appear to be their rarity. The author in using Fentazin in general psychiatric practice with both in and out patients over a period of approximately a year, and in larger doses than those used in the above cases, had never seen a severe reaction of this type. From the fact that we have had two such reactions out of a very small number of patients on the drug it seems that defective patients may be more liable to reactions from the drug than ordinary psychotics.

As regards the management of these severe side-effects when they do arise, the main danger in these cases would appear to be that of inhaling secretion during the time the neck muscles are in spasm. The management of Case 2 during the spasms was made much easier after the Atropine had begun to work, and I feel that if there is still considerable secretion after half an hour a further 1/100 gr. Atropine should be given. The second danger would be death following the severe physical exhaustion of the contractions. The severity of these is not apparently related to the dose given as in Case 1 the total dosage was many times that of Case 2 yet the spasms were by no means as alarming or severe. Should these contractions persist without ceasing over a long period then I feel the patient should be intubated with a cuffed tube, using a relaxant such as Succinylcholine and respiration could then be carried out using a Boyles machine.

The use of the anti-Parkinsonian drugs such as Ethopropazine or Benzhexal Hydrochloride, given parenterally may be of help, but, unfortunately, supplies of these in a suitable form were not available when the reactions occurred.

An interesting point raised in both cases is the fact that complete recovery occurred in a period of approximately 24 hours. This would appear to point to a fairly rapid elimination of the drug. Work on psychotics, however, using the Forrest Test for the measurement of the excretion of phenothiazines showed a relatively slow rate of elimination. Further investigation of this problem in defectives may be of help in understanding some of the failures of response which are experienced with phenothiazines by all working in this sphere.

SUMMARY

Two cases of severe reactions to Fentazin therapy are reported together with comments on their management.

ACKNOWLEDGMENT

I wish to thank Dr. M. Craft, Medical Superintendent of Balderton Hospital, for permission to publish these cases.

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Reviews

The Roots of Psychoanalysis and Psychotherapy. By S. A. SZUREK, M.D. Published by Charles C. Thomas, Springfield, Illinois, and simultaneously in the British Commonwealth of Nations by Blackwell Scientific Publications Ltd., Oxford, England. Pp. 144. Price 32s. 6d.

This interesting book opens challengingly, pointing out the variety of opinions held about the relationship of psychoanalysis to psychotherapy, some directly opposed to others. It then goes on to examine the interrelationship between psychoanalysis and psychotherapy under five selected headings:

1. The nature or the severity of the patient's disorder, or both.
2. The skill of the analyst or therapist.
3. The frequency of sessions.
4. The total number of sessions and the duration.
5. The therapeutic situation.

Dr. Szurek discusses his reasons for selecting these headings, and then proceeds to examine under each many points of great importance. It is especially interesting that in discussing Frequency of Sessions he stresses the importance of verbalizing and working through with the patient the reality factors which necessitate limiting the number of sessions. It is a pity that in the section under Duration of Therapy there is no mention of analogous reality problems, for certain workers have noted that the very conflicts concerning separation and ability to be on one's own can be highly significant foci for treatment when decisions to limit the duration of therapy are made.

The author's interest in Ferenczi's work is very obvious. There is a long description of analytic work; the usefulness of giving detailed attention to the patient's actual physical behaviour in the session is shown, but again he has not followed up Ferenczi's ideas on giving a termination date—ideas of course, which Ferenczi elaborated following Freud's work on this point.

Freud was the first to realize that the question of how to *treat* a patient is not important, but rather "what can I do *with* the patient towards the amelioration of his illness, disorder, or trouble", and Dr. Szurek makes this a central orientation point in his whole approach to psychoanalysis and psychotherapy, and he surveys it in great detail.

As more psychoanalysts involve themselves in therapy other than classical analysis, we can expect further progress of the kind Dr. Szurek has made. But already in this book he offers valuable pointers to improved techniques. He is to be congratulated in being able to cover adequately in a comparatively slim book, a very wide and complex field.

J. L. ROWLEY.

Mechanization of Thought Processes. Symposium at the National Physical Laboratory, 24-27 November, 1958. 2 Vols. H.M.S.O. Pp. 980. Price 50s.

The aim of this Symposium was to bring together the leading scientists in the study of all the many activities that today can recognizably be carried out both by the brain and by the computing machine. The topics included mechanical translation, learning, pattern recognition, problem solving, self-programming, and artificial thinking generally. The participants were mathematicians, psychologists, engineers, psychiatrists, physicists and physiologists.

Thirty-two papers were read and five machines demonstrated. The topics were grouped under the headings: General principles, Automatic programming, Mechanical

translation, Speech recognition, Learning in machine, Implications for biology, and Implications for industry.

No paper referred specifically to a psychiatric topic, though there was a continual irruption of suggestive ideas when the description of how a thought-process could normally be carried out evoked an image of the particular abnormalities of behaviour that would occur if the process went wrong. Those who are interested in the cybernetic aspects of brain function will find a wealth of suggestive ideas in these two volumes.

W. ROSS ASHBY.

Delinquency and Parental Pathology. By ROBERT G. ANDRY. Methuen & Co. Ltd., London, 1960. Pp. XV and 173. Price 21s.

In a foreword to this book, Dr. Hermann Mannheim points out that since Dr. John Bowlby first drew attention to "maternal deprivation" as a strong factor in producing serious and persistent delinquents, there has been a tendency amongst those responsible for the care of children to regard early separation of a child from his mother as an evil to be avoided at any cost. A more discriminating attitude has emerged in recent years, and the undue neglect of the role of the father, a perhaps unintended consequence of the Bowlby theory, has been pointed out.

The author, a clinical psychologist, concerned about this, gives the results of a painstaking field study, carefully checked by statistical methods, into the roles of *both* parents in the aetiology of delinquency. Using a questionnaire method in personal interviews, Dr. Andry examined 80 delinquent boys in a London Remand Home, aged between 10 and 15 years, and compared them with 80 matched non-delinquent boys from two London Secondary Modern Schools. He also examined both parents, using the same methods, of 30 of the delinquents and 30 of the controls as a check to the consistency and meaningfulness of the boys' replies. From this study, while sound data did not emerge on separation, he feels that there are strong indications that, compared with non-delinquents, delinquents experience less open and strong love from their parents and less adequate communication with them. They experience a more tense home atmosphere, a less adequate parental training and deviant behaviour is less known to and less adequately dealt with by the parents. In all this, the father especially took an inadequate role and this seemed to be more important than mother's role in differentiating delinquents from non-delinquents.

No extensive claims are made and the need for further research is pointed out; the author modestly suggests that perhaps the methods described here, with concomitant studies of parents' and children's attitudes to each other, might be used.

W. WARREN.

Research in Psychotherapy. Editors: ELI A. RUBINSTEIN and MORRIS B. PARLOFF. American Psychological Association, Inc. Pp. 293. Price 3 dollars.

This book consists of an account of the proceedings of a conference held in Washington in 1958 to take stock of the present state of research in psychotherapy. The conference and the publication of the proceedings were financed by a grant from the U.S. National Institute of Mental Health. There were about thirty psychiatrists and psychologists at the conference, representing almost as many approaches to psychotherapy. The papers and formal discussions are reproduced in full, while the report of the informal discussions has been abridged. Papers were read on the problems of controls in psychotherapy, on psychological and physiological methods for trying to study changes that occur in psychotherapy, and on methods of studying the interchange between therapist and patient. Discussion ranged over such topics as the goals and methods of conducting research, and on the selection of variables. In the last chapter the editors give a clear, succinct and critical account of the major issues considered at the conference.

The papers and the discussions indicate the difficulties of research in psychotherapy and the pitfalls associated with any method of research. Unfortunately, what does come through is that the state of research in psychotherapy, as discussed at this

conference, is a muddle. Whatever may be said by way of the value of their work in silencing those critics who accuse psychotherapists of not attempting to translate their results into the language of natural scientists, the failure of the participants to attempt to clarify the different ways in which each one uses basic terms can only confirm a belief in their unscientific attitude.

A very important question that was raised in discussion was whether or not all the participants shared a comparable picture of the term psychotherapy, but unfortunately this question was not followed up. One can say that in all areas of life where one person sets out to help another by talking, the interchange between them has some sort of outcome. This is so whether the relationship is a discussion between friends, a teacher guiding a pupil, a social worker advising a client, a priest admonishing a parishioner, or a doctor treating a patient. The psychiatrist however, often confuses the issue by not differentiating between two totally different approaches. Sometimes what he does differs little, apart from his having an increased amount of psychological understanding, from the work of the other groups of people just mentioned, except that he attaches to his work the dignity of the term psychotherapy. Sometimes, however, the trained psychotherapist does employ skilled techniques that really are unavailable to the others; for instance, when he actively employs his knowledge that mental illness derives from unsolved intrapsychic conflicts which are unconscious, when he actively tries to understand how these conflicts manifest themselves in the interview situation through the transference, and when he makes use of techniques such as interpretation of the transference. However, many of the workers who attended this conference are, while talking about psychotherapy, really trying to assess the routines of the former approaches.

The aims of therapy were not defined and it was clear that different workers had totally differing concepts. Numerous workers indicate that the aim of their treatment is the patient's health, but no satisfactory attempt was made to define this term. Barbara Wootton in her *Social Pathology and Social Science* has shown the confusion there is among psychiatrists when they use the word health. The word "interpretation" occurred from time to time with the implication that saying that an interpretative technique was used made the nature of the treatment self-evident. There was no indication of what was interpreted, when or how. The same sort of confusion surrounded theoretical concepts. The editors indicate that the conference showed very little interest in any assessment of the many different schools represented; because of this non-committal attitude, the nature of the therapists' work with their patients could not be brought out into the open.

The unrecognized collusions not to face these extremely painful areas have been paid for by more confusion. That things were felt to be far from satisfactory was revealed in the discussions, where so many of the participants felt quite desperate about the numerous conflicting views and attitudes. One cannot escape the conclusion that no amount of complex organized research can replace the need for detailed study of the meaningfulness to the patient of the therapist's endeavours, his interventions and his interpretations. There are centres in this country where this kind of study is being carried out. This book, however, does give a general indication of many aspects of the problems connected with research in psychotherapy.

ALEXIS BROOK.

Psychology of Personal Adjustment: Students' Introduction to Mental Hygiene. By FRED MCKINNEY. Third Edition. John Wiley and Sons, Inc., New York, 1960. Pp. 482.

This substantial volume is hailed by the publishers as "a best seller on student problems in the psychological and adjustment setting—now thoroughly revised and up-dated". The author, who is Professor and former Chairman of the Psychology Department at the University of Missouri, has drawn his material from 20 years' experience of counselling college students, and it is with their emotional needs and struggles towards self-realization that he is primarily concerned.

The manifold problems of life, leisure and love on the campus are sketched in a series of case histories, most of which are commendably brief. By contrast the intervening discussion is verbose and repetitive, and although the previous edition (1949) has been reduced by over 250 pages, the book would have benefited from a more ruthless resection of dead matter.

While rightly emphasizing the importance of creative outlets both within and outside one's chosen field, the author at times comes dangerously close to the spirit of Dale Carnegie, especially in his final recipe for mental health which mingles common-sense advice with moral exhortations ("Face your troubles" and "Be courageous in crises"). This may not worry the typical American student but it is likely to irritate his British counterpart. Moreover, although the scope of the book is wide, ranging from mnemonics to the choice of a mate, its quality is uneven and is apt to vary inversely with the level of abstraction. If the author is at his best when dealing with concrete and practical problems such as how to squeeze the most out of an hour's work, this is perhaps as it should be since his main purpose is to teach students how to live. The decision to include the extensive bibliography in a separate instructors' manual, *Teaching Personal Adjustment*, rather than in the present volume can be justified on similar grounds although it is inconvenient for the professional reader and does not make the reviewer's task any easier.

MICHAEL E. HUMPHREY.

An MMPI Codebook for Counselors. By L. E. DRAKE and E. R. OETTING. Minnesota University Press; Oxford University Press, London. 1960. Pp. 140. Price 30s.

In this book the authors set out to construct hypotheses from MMPI profiles for the purpose of counselling. Whereas the original MMPI scales were derived from studies of clinical populations, the present studies, including the addition of a "Social Introversion-Extroversion" scale, were based on profiles of some 4,000 male and female students at the University of Wisconsin, a population which the authors regard as comprising "relatively normal persons". The authors hold that the behaviour which the counsellor is trying to understand or to predict is too complex to be measured by a single scale or even a combination of scales. They therefore investigated the way in which the scales operated in patterns. Frequency tables of high and low codings of scales and of the combinations of such scale codings were computed for the total group as well as for sub-groups, the latter being established in accordance with the personality characteristics available from the counsellor. A comparison of frequencies of occurrence of each pattern could thus be made between the sub-group and the total group to determine statistically whether the pattern could be accepted as being differential.

The cautiousness and modesty with which the authors present their findings deserve praise and sympathy. The same spirit prevails in the introductory chapter on the use of psychometric data in counselling. Much is also to be said for the authors' attitude to adopt a middle course between those counsellors who reject the use of psychometric data altogether and those who rely on it exclusively. However, the all-important problem of the effect of administration of tests on the "rapport" between counsellor and student is merely mentioned but not dealt with in any detail.

The code book proper, containing 84 pages, is divided into a male and female section. It remains to be seen whether it can provide the counsellor with the help the authors hope for. Obviously its use is limited through being standardized on a student population.

F. H. STRAUSS.

The Education of Slow Learning Children. By A. E. TANSLEY and R. GULLIFORD. Routledge & Kegan Paul Ltd., London, 1960. Pp. 255. Price 28s.

This book is intended for teachers of "slow learning" children in primary, secondary or special schools for the "educationally subnormal"; it summarizes in straightforward terms the intellectual, emotional and physical characteristics of very

backward children, with practical advice on teaching methods. The authors rightly point out that "co-operation and consultation between doctors, psychologists, teachers and others who know the child seem essential, if only because physical, social and psychological problems are so often associated with educational backwardness". They are clearly very experienced in their field and describe, for instance, the characteristics to be expected from the brain damaged child. On the other hand, it is perhaps inevitable, following the report of the Underwood Committee, that "maladjustment" is described as a sort of generic term and as though it were a diagnosis in its own right. Although written for teachers, Child Psychiatrists in training would gain much useful information on the educationally subnormal child as seen in the school setting.

W. WARREN.

Cerebral Dominance and Its Relation to Psychological Function. By O. L. ZANGWILL. Oliver and Boyd, Edinburgh, 1960. Pp. 31. Price 10s. 6d.

This is the nineteenth Henderson Trust Lecture, and Professor Zangwill, considers the relationship of handedness and the cerebral control of speech. Having reviewed previous work and his own studies in this field, he suggests that there is a category of individuals in whom language and kindred processes are imperfectly lateralized to either cerebral hemisphere and who may in consequence be said to lack cerebral dominance. They comprise some of those designated as left-handed together with a number who appear to lack strong and consistent lateral preferences. They may be described as "ambilateral" and may include a number of right-handed individuals with a covert sinistral tendency. It is felt that such does not imply any abnormality in psychological development, but that the possessor of ambilaterality is particularly vulnerable to the effects of stress.

Professor Zangwill goes on to study the problem of specific educational disability in children and its relation to cerebral dominance. He considers that in the ambilateral child, the proper development of reading and writing, of spatial judgment and directional control, is relatively easily disturbed by accidents of circumstance. Such may include minimal brain injury at birth, predisposition to epilepsy, the after-effects of childhood illness, or even problems in psychological attachment at home or at school. He ends by pointing out that although the problem of cerebral dominance is far from solved, it has perhaps been in some measure clarified by recent studies; this Henderson Trust Lecture certainly helps to make these matters clearer for the reader.

W. WARREN.

Psychological Appraisal of Children with Cerebral Defects. By EDITH MEYER TAYLOR. Harvard University Press, The Commonwealth Fund, 1959. Pp. XVII and 499. Price 68s.

Dr. Taylor joined the Neurological Division of the Children's Hospital, Boston, Massachusetts, in 1943. Following on from the work of her predecessor, Dr. Elizabeth Lord, she has built up over the years considerable practical knowledge of the psychological assessment of children with cerebral defects. This includes long-term observations of the children concerned, and so opportunity to check her earlier findings and to re-appraise her techniques. This book is the result of her experience; practical rather than theoretical, it describes the psychological evaluation of the potentialities and prospects of children with neurological handicaps and how the findings can be interpreted and used. She points out that the approach to these children needs to be flexible and related to the total situation. Emphasis is placed on the unity of the examination process with careful judgment of what test scales are selected to yield the least equivocal results in the particular circumstances. Reports need to be designed to be of help to those others who are concerned in treating or training the patients. With these and other practical points in mind, the assessment of a number of children with differing kinds of neurological handicap is described in detail. Designed for the guidance of the clinical psychologist who may be relatively inexperienced in this

field, the psychological methods used are familiar ones; new methods are not introduced and there is little attempt to enquire further into what is still a relatively unexplored subject, that is the assessment of brain damage.

W. WARREN.

Personality Patterns of Psychiatrists. By ROBERT R. HOLT, Ph.D., and LESTER LUBORSKY, Ph.D. Publishers: Basic Books, Inc., New York.

This treatise, in two volumes, is extremely technical and too detailed for any but the most highly specialized of readers. Nevertheless it reports a careful, self-critical and important piece of research; and should be of value as a reference manual for academic psychiatrists and psychologists who are interested in large-scale selection of candidates for training in psychiatry. It gives an account of a pioneer attempt to evaluate and compare different methods used for the selection of medically qualified candidates for training at the Menninger School of Psychiatry and to investigate which character traits were most essential for success in the practice of psychiatry.

The first volume is divided into four sections; the first describes the history of the project and the awakening of public interest in mental health in America. The physicians who applied for training were mainly from middle-class homes and a large proportion had had experience of chronic mental or physical ill-health in their family background; their main interest was in psychotherapy and psycho-analysis, as opposed to physical methods of treatment.

The second section discusses the theory of the research and gives a long history of "Personnel Selection". The techniques and scope of the various tests are described in great detail. The results obtained *via* a specially structured interview are compared with those based on statistically validated tests and with the results of the School Admission Committee. It was acknowledged that the Committee's forecasts were often the most accurate. They did have more data available but it is shown that, after a certain point, an increase in the amount of data merely confuses; the reader may feel the truth of this when faced with the amount of data in these volumes! The aim of all three methods is to select applicants who would be able to complete the three years' training programme; pass the examination of the American Board of Psychiatry and Neurology, and succeed in psychiatric practice. The reaction of one trainee to the battery of tests and interviews is given in detail.

The third section surveys the opinions of clinical psychiatrists, psychoanalysts and other experts upon the personality factors required in a competent psychiatrist, it would appear that the main requirements were, to be likeable; to have warmth; integrity; a wide experience of life; and a not too intellectual approach; to be able to inspire confidence; to be tactfully dominating and above all, to have intuitive understanding of the patient and his problems and to gain rapport with him.

The fourth section is perhaps the most valuable and contains advice on selection methods. There is an explanatory note for readers who know little of statistics, which however may not help those who are not mathematically minded.

The second volume consists mainly of tabulated test results; descriptions of tests, and explanatory notes related to Volume I. Among points made are, that the Veterans Association, very rightly, refuse to allow undue experimentation with their patients; that most practical knowledge seemed to be gained in the first year of study; that interests and curiosity about people were more reliable incentives than "an urge to heal"; that the I.Q. could range between 120 and 137, and that at least 37 per cent. of rejected candidates succeeded in qualifying elsewhere.

There were some interesting findings in both volumes on emotional stability and the need for psychiatric treatment amongst trainees. In general it was impossible to forecast which of the accepted candidates would do best in the later stages of training and practice, because this depended on the individual's capacity for emotional and mental growth under the stimulus of training and experience.

W. A. H. STEVENSON.

The Nature of Stress Disorder, Conference of the Society for Psychosomatic Research. Hutchinson Medical Publications, London, 1959. Pp. 298. Price 25s.

The great value of this report lies in the multidisciplinary approach and in the honesty with which established knowledge and areas of ignorance were presented. The Society for Psychosomatic Research is a working party limited to thirty-five members. A number of guests had been invited to this conference. Some speakers use the term stress disorders for psychosomatic diseases, while others favoured a more general concept. Experimental work was discussed, but the emphasis was clinico-psychological. There was an interesting symposium on "stress and occupation" which included a report on psychiatric and psychosomatic disorders in a population of university students. Studies by psychoanalysts were presented side by side with contributions by geneticists, endocrinologists and by experts in public health. The standard of the papers and of the discussions was remarkably high. The proceedings were chaired by Charles Newman, J. Z. Young, Leslie Banks, A. V. Neale, Fraser Roberts and John Hambling, who is the President of the Society. John Wisdom provided a brilliant summing-up in which he distinguished between proven facts, theory and speculation. He discussed the various concepts of stress employed in this conference. Everybody who wants to clarify his thoughts about stress and psychosomatic disorder will benefit from reading this book if only by finding his own difficulties with these concepts clearly formulated.

E. STENGEL.

Operational Values in Psychotherapy. By DONALD D. GLAD, Ph.D. With Portions contributed by VIRGINIA M. GLAD, Ph.D., and ROBERT H. BARNES, M.D. Oxford University Press, 1959. Pp. 326. Price 68s.

This book consists essentially in a detailed examination of four systems of psychotherapy: Psycho-analysis (Freud), Interpersonal Psychiatry (Harry Stack Sullivan), Dynamic Relationship Therapy (Otto Rank), and Client-centred Therapy (Carl Rogers). The author compares the influence of these four systems on the point of view and actions of the therapist; particularly on (1) what he *selects* from the patient's communications; (2) what he *infers* from the selected data; (3) what factors in mental functioning he *values* and calls mental health; and (4) what kind of *interventions* he makes. The author's main thesis is that each particular system calls out in the patient responses characteristic of the system itself. This leads to two important consequences. The practical consequence (which is emphasized in a commentary by Robert H. Barnes forming the last chapter of the book) is that different kinds of patient may be suitable for different systems. Dr. Barnes suggests that this possibility should be borne in mind in assigning patients for treatment. The main point of the book, however, is the theoretical consequence. This, perhaps overstated in the book, is better put in the form of a question: how far does the process of psychotherapy consist simply in the "conditioning" of the patient to adopt the therapist's values, and thus how far does every theory of psychotherapy tend to prove itself automatically?

The author has attempted something very ambitious, namely to master the theory and technique of these four systems, and to describe each accurately and dispassionately. To a large extent he appears to have succeeded (though the reviewer naturally cannot be a reliable judge of this for systems other than his own). It is a measure of the author's lack of bias that were it not for a reference to his "own analyst" one would be quite unable to guess which system he himself belonged to—and even this, presumably, is ambiguous.

Criticisms of secondary importance are that the book is not easy to read because the writing is rather discursive; the author's views on the process of psychotherapy are perhaps somewhat superficial; there are a number of illustrative diagrams which seem to obscure rather than to illuminate; and the same point tends to be repeated over and over again in different places. Against this it must be said that the main thesis can bear a good deal of repetition. It brings home more than ever the need for a wider view than can be provided by any single system of psychotherapy; and the

need, in assessing any piece of research, to ask how far the evidence may only be valid for the particular kind of patient selected and the particular system which the therapist practises.

The future of psychotherapy as a scientific subject depends on our ability to find ways of presenting relevant and valid evidence in such a form that various alternative explanations may be considered and evaluated, not only by the authors themselves, but independently by the reader. It is the evaluation which is difficult, since though the evidence itself may be reliable, there may be many pitfalls in its interpretation. Dr. Glad has drawn attention to one such pitfall, and his book may therefore be regarded as a welcome contribution to good sense in psychotherapy.

DAVID MALAN.

Journal of Child Psychology and Psychiatry and Allied Disciplines. Joint Editors: C. B. HINDLEY, ELIZABETH IRVINE and EMANUEL MILLER. Volume 1, No. 1, January, 1960. Pergamon Press, Oxford.

Child psychiatrists have awaited with interest the advent of this new journal and they should not be disappointed with the first number. The editors are well known and the impressive advisory board of international scope; they have produced an attractive looking and well printed journal containing a number of papers of a uniformly high standard.

The editors give something of the history of its emergence. "At the 1955 Toronto meeting of the International Congress of Child Psychiatry and Allied Disciplines, the British participants felt the need to set up an organization in their own country. Whilst the original nucleus was conceived in terms of the members of a child guidance team, the resulting Association of Child Psychology and Psychiatry adopted wider aims, including the furtherance of the fundamental study of the child and the family. Any serious student, from any of the disciplines which can contribute to this aim, was therefore welcomed to membership." As far as this journal is concerned, a primary purpose of the new association is "to bring together original papers concerned with the child, from such diverse disciplines as psychiatry, psychology, paediatrics, psychoanalysis, social case work and sociology". In the first number the accent is on psychiatry, as the editors point out. They add that as it becomes more widely known, they will be able to communicate researches and opinions which will justify their aims as a scientific journal conveying all aspects of child study.

A good start has been made and it is hoped that the editors will, at least as far as child psychiatry is concerned, not be short of material of an equally high standard in the future. Judging from the past, however, the number of worth-while articles submitted for publication by child psychiatrists in this country seems to have been comparatively small. Perhaps this new journal will be a stimulus and if in further numbers the accent is more on the other aspects of child study, at least Child Psychiatry should be able to maintain a reasonable quota.

W. WARREN.

The Sixth Sense. An Enquiry into Extra-sensory Perception. Chatto & Windus, London, 1959. Pp. 224. Price 21s.

The facts of the so-called "supernatural" remain the most difficult matters on which the scientist who studies the brain has to form an opinion. In their mass they offer proofs of the supernatural far exceeding in size and detail the proofs available for many well known and accepted phenomena, such as that for the deviation of light by gravitation, or the causation of general paralysis by the spirochaete. Many of those people who dismiss the supernatural as nonsense have never come into contact with the full weight of the evidence. Unfortunately, this vast mass of evidence is accompanied by refutations as vast and detailed, which are themselves countered again, and so on until the judgment falters and one is left, usually, believing in one's first hunch!

I can at least say, however, that Mrs. Heywood's book gives an excellent survey

of the evidence. Though not exhaustive, it is none the less surprisingly broad in its range, and there is little worth-while evidence that is not mentioned. The subject is treated sympathetically, yet with scrupulous impartiality. Readers who want a polemic for one side or the other will be disappointed, but those who would like to see what the evidence is when it is displayed to its best advantage will find the book well worth reading.

It is certainly one of the best surveys that have appeared for many a year.

W. ROSS ASHBY.

Die Beginnende Schizophrenie. By K. CONRAD. Georg Thieme, Stuttgart, 1958.

In this book Conrad has tried to explain the origin of and inter-connection between the different delusional and paranoid phenomena which occur in acute schizophrenic shifts. Before discussing his ideas it is necessary to describe the background against which they have developed.

Jaspers was originally responsible for the intensive interest which the German psychiatrist had in so-called primary delusional phenomena. He introduced Husserl's concepts of 'understanding' and 'explaining' psychology into psychiatry. Briefly Husserl believed that in psychology we have two different types of connection between events. There are causal connections which are established on the basis of observation and experiment. These connections form the basis of 'explaining' psychology. The other variety of connection is the understandable connection. This arises because a psychological event can arise out of another psychological event in a way which we can understand. Thus for example we can understand why a man who is being ridiculed becomes angry and aggressive. Such an understandable connection between two psychological events can be called a genetic understandable connection because it allows us to understand how one psychological event arises out of another.

Jaspers used this idea of understandable connections in his analysis of the psychopathology of the delusion. He divided delusions into two kinds—delusion-like ideas and true delusions. Delusion-like ideas are delusions which arise in an understandable way from some other well-known psychological event. Thus a depressed patient develops delusions of guilt because he is depressed and feels useless. The true delusion arises from a primary delusional experience which cannot be understood. The new signification emerges in connection with some psychological event, but cannot be derived from it. At the time when Jaspers wrote the prevalent type of psychology was that of Wundt, which tried to dissect all phenomena into their basic elements and basic functions. Consequently a large number of primary delusional experiences were isolated, such as delusional perception, delusional state of consciousness, delusional memory, delusional presentation and so on.

The older German workers who followed Jaspers described and analysed delusional experiences in great detail. However they were influenced by the prevailing psychology and did not attempt to explain these primary experiences. It is necessary to consider in some detail the three most important delusional experiences, viz. delusional mood, sudden delusional ideas (autochthonous delusions) and delusional perception.

In delusional mood the environment appears to be changed in a strange threatening way, but the significance of the change cannot be understood by the patient. A delusion may crystallize out of this mood and when it does the tense, anxious, unpleasant feeling usually disappears. A sudden delusional idea is one which arises abruptly in the patient's mind without any preparatory thoughts. Delusional perception occurs when an abnormal significance, usually in the sense of self-reference, is attributed to a normal perception in the absence of any emotional or logical reason. This phenomenon has been described and discussed more than the others and Kurt Schneider has considered it to be diagnostic of schizophrenia. Conrad has pointed out the need for a convenient designation for all these delusional experiences from which an adjective could be derived. Since in all these experiences something is becoming manifest to the patient Conrad suggests the word *apophany*, which is the Greek for the becoming

manifest, as the suitable designation. The adjective *apophanous* can be derived from this term so that one can talk of apophanous ideas, moods, perceptions and so on.

Marussek has examined the concept of delusional perception and attempted to explain it in terms of Gestalt psychology. The older investigators were all agreed that delusional perception was a disorder of thought and that perception was not altered in this experience. Marussek pointed out that there were two different types of delusional perception. In one the abnormal significance is dependent on a play on words. Thus a patient heard a floorboard squeak, he looked down and saw the linoleum. He said to himself "Lino" and immediately the thought "Don't lie" came into his mind. This signified that he was being warned not to lie. This sort of play on words is similar to the verbal tricks used by the obsessional ruminator when he finds indications of his obsessional thoughts in his environment. In the other type of delusional perception Marussek believes that there is a perceptual change which consists of a loosening of the coherence of perception which leads to the undue prominence of essential properties of the object. Essential properties are expressions of the essence of the object. They are, for example, expressed in the adjective in the following phrases—the laughing man, the sleeping village, and the threatening mountain. If the essential properties gain undue prominence in delusional perception they naturally have a new significance for the patient.

Conrad accepts Marussek's ideas and weaves them into a theoretical structure which is an attempt to correlate the variegated symptomatology of the acute schizophrenic shift. He bases his interpretations on his experiences with a group of 107 acute schizophrenics, whom he looked after in a German military hospital in Germany in the years 1940-1941. He believes that five phases can be seen in a typical shift. These are:

1. The Tremor.
2. The Apophanous Phase.
3. The Apocalyptic Phase.
4. The Consolidating Phase.
5. The Residual Phase.

The word *tremor* is German stage slang for the stage fright which occurs before the actor makes his appearance. In the tremor the patient experiences a loss of freedom so that he feels hemmed in and unable to communicate with his environment. Senseless actions occur and these were particularly noticeable in Conrad's patients because they led to conflict with authority. Thus one patient held his ears when his company commander shouted at him. Severe anxiety may occur, but depression is also common with marked ideas of guilt and disgust with life. In other patients there was a general feeling of suspicion, which pervaded all social contacts and led these patients to feel that there was something else behind all their experiences. Finally, delusional mood occurs, in fact Conrad believes it occurs in nearly all early schizophrenics but they are often not able to describe it. The tremor may last a very short time or for several months before the apophanous phase begins. Sometimes the illness subsides without any further development.

The apophanous phase can be divided into two. There is the apophany of external space, that is external events acquire a new significance and there is apophany of internal space in which psychic events not directly related to the external world acquire a new significance. In external apophany an event acquires a special meaning for the patient and, unlike a normal person who accidentally believes that some external event has some connection with him, he is unable to put to himself the alternative that the event has no significant attention for him. Delusional perception is a common external apophanous experience. Conrad distinguishes three stages of delusional perception. In stage 1 the perceived object indicates to the patient that it has some significance for him, but he cannot say to what extent. This is pure apophany. In stage 2 the perceived object indicates to the patient that it has a significance for him and he knows immediately the extent of this. For example, it has been put there

to test him or observe him. There are the made or prefabricated experiences of Schneider. The third stage occurs when the perceived object signifies something quite definite. The essential properties have come into prominence. This is delusional perception in the strict sense.

Misidentification of persons often occurs in the apophanous phase, so that unknown persons are recognized as friends or acquaintances and persons well known to the patient appear to be unknown. This can be explained by the undue prominence of essential properties which cause the patient to misidentify acquaintances and strangers.

All these experiences give the patient the impression that he is in the centre of a changed world. On the other hand some of Conrad's patients had the experience of omnipotence and knew that their actions influenced the world. Thus one patient believed that as he wished he caused bombs to fall on England. There is a quality of accomplishment in this experience, since both wishing and bombing are activities in which something is made to fall, so that they both have a common essential property of activity. The experience of a special effect of the constituents of the world on the patient which is best seen in delusional perception is coupled with an experience of a reciprocal effect of the patient on objects of the world. In other words the essential properties of the patient's own actions may become important for the world as he experiences it. The patient may have the experience that he is in the centre of the world, that everything revolves round him. Conrad calls this *enastrophie*.

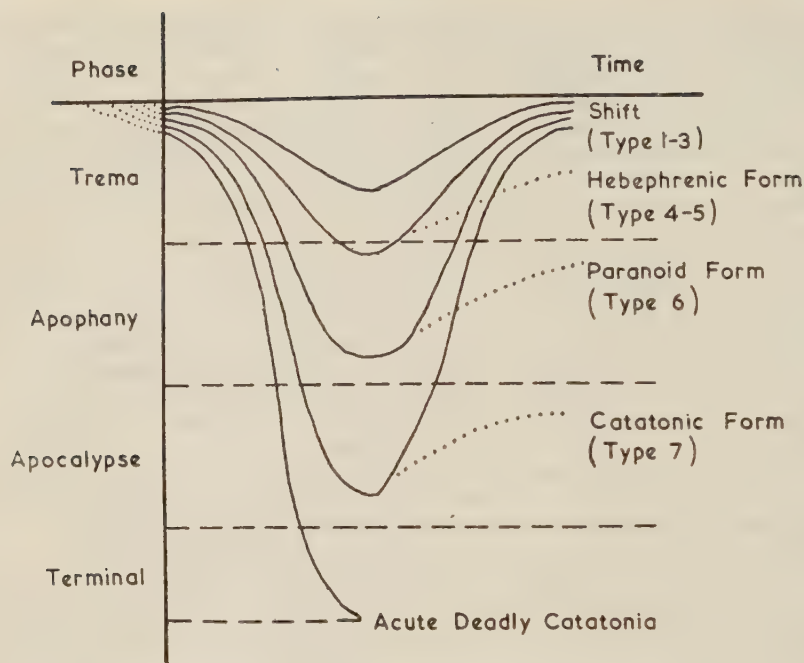
Apophany may only affect external space or internal apophany may not occur for some time. It seems as if there is a barrier which stops the process from spreading quickly from the sensory aspects to the representational aspects of psychic life. Once apophany affects internal space there is a de-differentiation of field structure. Thus freely rising memory images lose their connection with the total field and become delusional inspirations. In thought broadcasting the patients' thoughts become manifest in his environment and this can be regarded as the reverse aspect of delusional perception where a perception becomes manifest to the patient. The loosening of the coherence of representational aspects of psychic life leads naturally to the patient hearing his own thoughts spoken aloud, so-called *Gedankenlautwerden*. When all personal indication of the thoughts is lost then hallucinatory voices occur. Bodily hallucinations can be explained as apophany affecting bodily sensations and the body image.

The illness may stop at the apophanous phase, but if the schizophrenic process is very severe the loosening of coherence of perception and representation may proceed to complete chaos. Psychic life becomes fragmented and the apocalyptic phase or catatonia is present. The release of representation of bodily sensations and movements leads to the motor disorder. As sense continuity is destroyed, only fragments of the total experience can be remembered subsequently. In rare cases the apocalyptic phase may end in death.

Usually the phase of consolidation sets in after a few weeks or months. The apophany dies away and the patient may finally gain insight into his strange experiences. Finally the residual phase is reached. Here no active symptoms are present, but the patient feels less capable than before. Often this change is much more apparent to the patient than to his fellows. Conrad considers that every individual has his own particular ability to direct and apply his energies or in other words has his own energy potential. In the residual phase this potential is lower than normal.

Conrad has described seven different types of course of illness which are illustrated in the diagram overleaf. These are:

- Type 1. The process does not pass beyond phase 1 and only abates on phase 2. It subsides in a few weeks. The loss of energy potential is minimal.
- Type 2. The process passes through phase 1, enters phase 2 and then subsides after a few weeks. Loss of energy potential is slight.



VARIETIES OF ACUTE SCHIZOPHRENIC SHIFTS (AFTER CONRAD)

- Type 3. Phases 1 and 2 are passed through and phase 3 is touched on. The process then subsides.
- Type 4. Phases 1 and 2 are quickly passed through without the psychosis being recognized. A marked loss of energy potential occurs and the residual state may make adaptation very difficult.
- Type 5. Process does not pass beyond phase 1 but a severe reduction of energy potential occurs.
- Type 6. Process reaches phase 2 and it is arrested there.
- Type 7. The process reaches phase 3 and is arrested in that phase. This results in a severe loss of potential.

Conrad believes that schizophrenia is due to a disorder of the nervous system. He has used Gestalt theory to explain the form and relationship of symptoms in acute schizophrenic shifts.

This is the first fresh approach to the psychology of schizophrenia for many years. It is extremely stimulating and worthy of careful consideration.

FRANK FISH.

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(R.) indicates a *Review*; the title of the book reviewed is followed by the author's name.

(E.) indicates the *Epitome* section; the title of the epitome is followed by the author's name.

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